DISSERTATION

A STUDY ON BIOCHEMICAL PARAMETERS ESR,CRP, URIC ACID AND FIBRINOGEN FOR PREDICTION OF FUNCTIONAL OUTCOME IN PATIENTS WITH ISCHEMIC STROKE AT GOVERNMENT STANLEY HOSPITAL CHENNAI – 600 001.

Dissertation Submitted to

THE TAMILNADU DR. M.G.R. MEDICAL UNIVERSITY
CHENNAI – 600032.

In partial fulfillment of the Regulations
for the Award of the Degree of

M.D. BRANCH - I
GENERAL MEDICINE
APRIL 2015

DEPARTMENT OF GENERAL MEDICINE
GOVT. STANLEY MEDICAL COLLEGE & HOSPITAL
CHENNAI - TAMILNADU

CERTIFICATE BY INSTITUTION

This is to certify that **Dr. VINOD KUMAR. R,** Post - Graduate Student (MAY 2012 TO APRIL 2015) in the Department of General Medicine STANLEY MEDICAL COLLEGE, Chennai- 600 001, has done this dissertation on "**A STUDY ON BIOCHEMICAL PARAMETERS ESR,CRP, URIC ACID AND FIBRINOGEN FOR PREDICTION OF FUNCTIONAL OUTCOME IN PATIENTS WITH ISCHEMIC STROKE AT GOVERNMENT STANLEY HOSPITAL CHENNAI – 600 001".** under my guidance and supervision in partial fulfillment of the regulations laiddown by the TamilnaduDr.M.G.R. Medical University, Chennai, for M.D. (General Medicine), Degree Examination to be held in April 2015.

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DECLARATION

I **Dr. VINOD KUMAR. R** solemnly declare that I carried out this work on "**A STUDY ON BIOCHEMICAL PARAMETERS ESR,CRP, URIC ACID AND FIBRINOGEN FOR PREDICTION OF FUNCTIONAL OUTCOME IN PATIENTS WITH ISCHEMIC STROKE AT GOVERNMENT STANLEY HOSPITAL CHENNAI – 600 001**" in the Medical OPD, Medical wards and IMCU of Government Stanley Hospital during the period January 2014 to September 2014. I also declare that, this bonafide work or a part of this was not submitted by me or any other for any award, degree, or diploma to any other university, board either in India or abroad.

This is submitted to The Tamilnadu Dr.M.G.R. Medical University, Chennai in partial fulfilment of the rules and regulation for the M.D. Branch I, General Medicine Degree examination

DR.VINOD KUMAR. R

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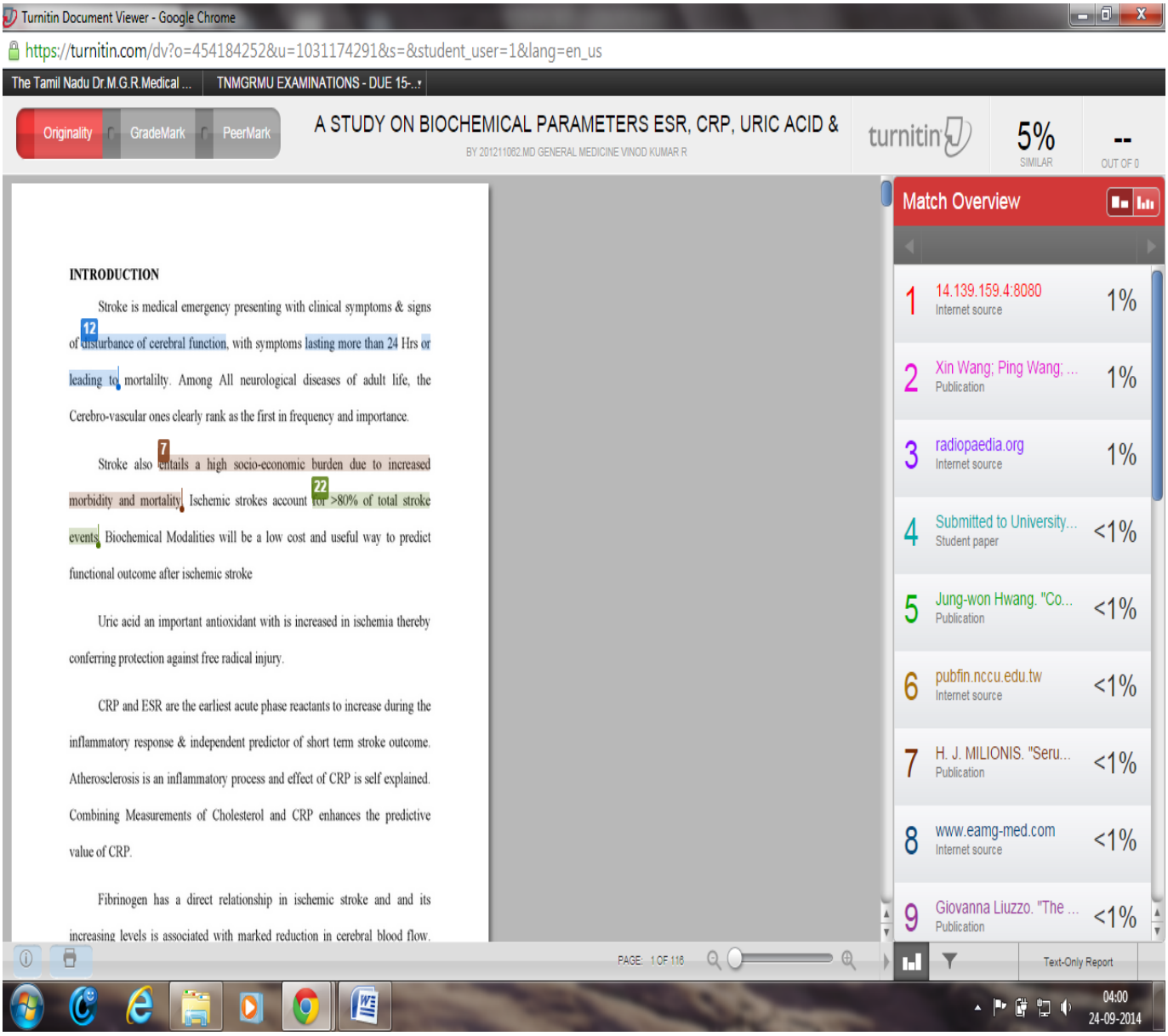
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INTRODUCTION
Stroke is medical emergency presenting with clinical symptoms & signs of disturbance of cerebral function, with symptoms lasting more than 24 Hrs or leading to mortalilty. Among All neurological diseases of adult life, the Cerebro-vascular ones clearly rank as the first in frequency and importance.
Stroke also entails a high socio-economic burden due to increased morbidity and mortality. Ischemic strokes account for >80% of total stroke events. Biochemical Modalities will be a low cost and useful way to predict functional outcome after ischemic stroke
Uric acid an important antioxidant with is increased in ischemia thereby conferring protection against free radical injury.
CRP and ESR are the earliest acute phase reactants to increase during the inflammatory response & independent predictor of short term stroke outcome. Atherosclerosis is an inflammatory process and effect of CRP is self explained. Combining Measurements of Cholesterol and CRP enhances the predictive value of CRP.
Fibrinogen has a direct relationship in ischemic stroke and and its increasing levels is associated with marked reduction in cerebral blood flow.
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CONTENTS

ABBREVIATIONS

SHT	SYSTEMIC HYPERTENSION
DM	DIABETES MELLITUS
CVA	CEREBRO VASCULAR ACCIDENT
TIA	TRANSIENT ISCHEMIC ATTACK
MI	MYOCARDIAC INFARCTION
ECG	ELECTRO CARDIO GRAM
EEG	ELECTRO ENCEPHALOGRAM
CT	COMPUTERISED TOMOGRAPHY
MRI	MAGNETIC RESONANCE IMAGING
ADL	ACTIVITIES OF DAILY LIVING
FLP	FASTING LIPID PROFILE
SUA	SERUM URIC ACID
CRP	C REACTIVE PROTEIN
ATP	ADENOSINE TRI PHOSPHATE
ESR	ERYTHROCYTE SEDIMENTATION RATE
CAD	CORONARY ARTERY DISEASE
CKD	CHRONIC KIDNEY DISEASE
RA	RHEUMATOID ARTHRITIS
SBP	SYSTOLIC BLOOD PRESSURE
DBP	DIASTOLIC BLOOD PRESSURE
IL	INTERLEUKINS
TNF	TUMOUR NECROSIS FACTOR
DVT	DEEP VEIN THROMBOSIS

AIMS AND OBJECTIVES:

1. TO STUDY THE BIOCHEMICAL PARAMETERS URIC ACID CRP ESR FIBRINOGEN IN ISCHEMIC STROKE PATIENTS AT GOVERNMENT STANLEY HOSPITAL

2. TO ASSESS FUNCTIONAL OUTCOME IN THESE PATIENTS USING BARTHEL INDEX AT ADMISSION AND AT DISCHARGE

MATERIALS AND METHODS

PLACE OF STUDY:

DEPARTMENT OF GENERAL MEDICINE, MEDICAL OPD, MEDICAL WARDS AND IMCU, STANLEY MEDICAL COLLEGE AND HOSPITAL, CHENNAI.

DURATION:

JAN 2014 TO SEP 2014.

STUDY DESIGN:

PROSPECTIVE OBSERVATIONAL STUDY

SAMPLE SIZE: 75

PATIENT SELECTION:

1. **ANY PATIENT COMING WITH SYMPTOMS SUGGESTIVE OF STROKE TO MEDICAL OPD MEDICAL WARDS AND IMCU.**
2. **Proven by Imaging as Ischemic Stroke.**

EXCLUSION CRITERIA:

1. **Hemorrhagic stroke patients**
2. **Patients with any source of Sepsis /acute infectious Disease**

3. **Patients presenting after 72 hours of onset**
4. **Patient with Ischemic Heart disease**
5. **Patient with any form of Arthritis**
6. **Recent Trauma burns Surgery**

METHODOLOGY:

Patients coming with symptoms suggestive of Stroke to OPD/admission unit/IMCU from Jan 2014 to September 2014 are included in the study keeping in mind the exclusion criteria mentioned above. Patients will be subjected to symptom analysis, clinical examination, laboratory investigations and Imaging studies. The final analysis will be made at the end of the study to achieve the fore mentioned goals.

CONCLUSION:

CRP apart from being an inflammatory marker has also been found to be a highly sensitive, non specific and an independent risk factor for prediction of Ischemic stroke. Similarly ESR, fibrinogen, Uric acid have also been found to be useful as early indicator of prognosis in Stroke patients.

The present study is done without any haste involving the above four parameters to predict the outcome among stroke patients. This study correlates with the previous studies done by eminent people as quoted by my citations

Inclusion of these tests in patients with acute stroke provides clinicians with a low cost and useful way to predict functional outcome after ischemic stroke, as measured by Barthel index which has been proved to have a strong correlation with inflammatory markers.

KEY WORDS: ISCHEMIC STROKE, INFLAMMATORY MARKERS, BARTHEL INDEX, FUNCTIONAL OUTCOME.

INTRODUCTION

Stroke is medical emergency presenting with clinical symptoms & signs of disturbance of cerebral function, with symptoms lasting more than 24 Hrs or leading to mortalilty. Among All neurological diseases of adult life, the Cerebro-vascular ones clearly rank as the first in frequency and importance.

Stroke also entails a high socio-economic burden due to increased morbidity and mortality. Ischemic strokes account for >80% of total stroke events. Biochemical Modalities will be a low cost and useful way to predict functional outcome after ischemic stroke

Uric acid is an important antioxidant increased in ischemia thereby conferring protection against free radical injury.

CRP and ESR are the earliest acute phase reactants to increase during the inflammatory response & independent predictors of short term stroke outcome. Atherosclerosis is an inflammatory process and effect of CRP is self explained. Combining Measurements of Cholesterol and CRP enhances the predictive value of CRP.

Fibrinogen has a direct relationship in ischemic stroke and and its increasing levels is associated with marked reduction in cerebral blood flow. Inclusion of these tests in patients with acute stroke provides clinicians with a low cost and useful way to predict functional outcome after ischemic stroke which in turn is measured by Barthel index.

REVIEW OF LITERATURE

STROKE

DEFINITION: "Rapidly developing clinical signs of focal(or global) disturbance of cerebral function with symptoms lasting 24 hours or longer or leading to death with no apparent cause other than of vascular origin". Stroke manifests by various neurological signs and symptoms depending on extent, area of involvement and the underlying causes. These include coma, hemiplegia, paraplegia, monoplegia, cranial nerve palsy, speech disturbance and sensory impairment etc. Of these hemiplegia is the most common presentation, seen in about 90% of patients.

Epidemiology

A WHO collaborative study in 12 countries showed that the incidence rates of stroke ranged from 0.2 to 2.5 per 1000 population per year. Analysis of data on various studies shows that about 2 % of cases in hospital, 4.5 % medical patients & 20 % of admissions in neurology are due to Stroke. The main

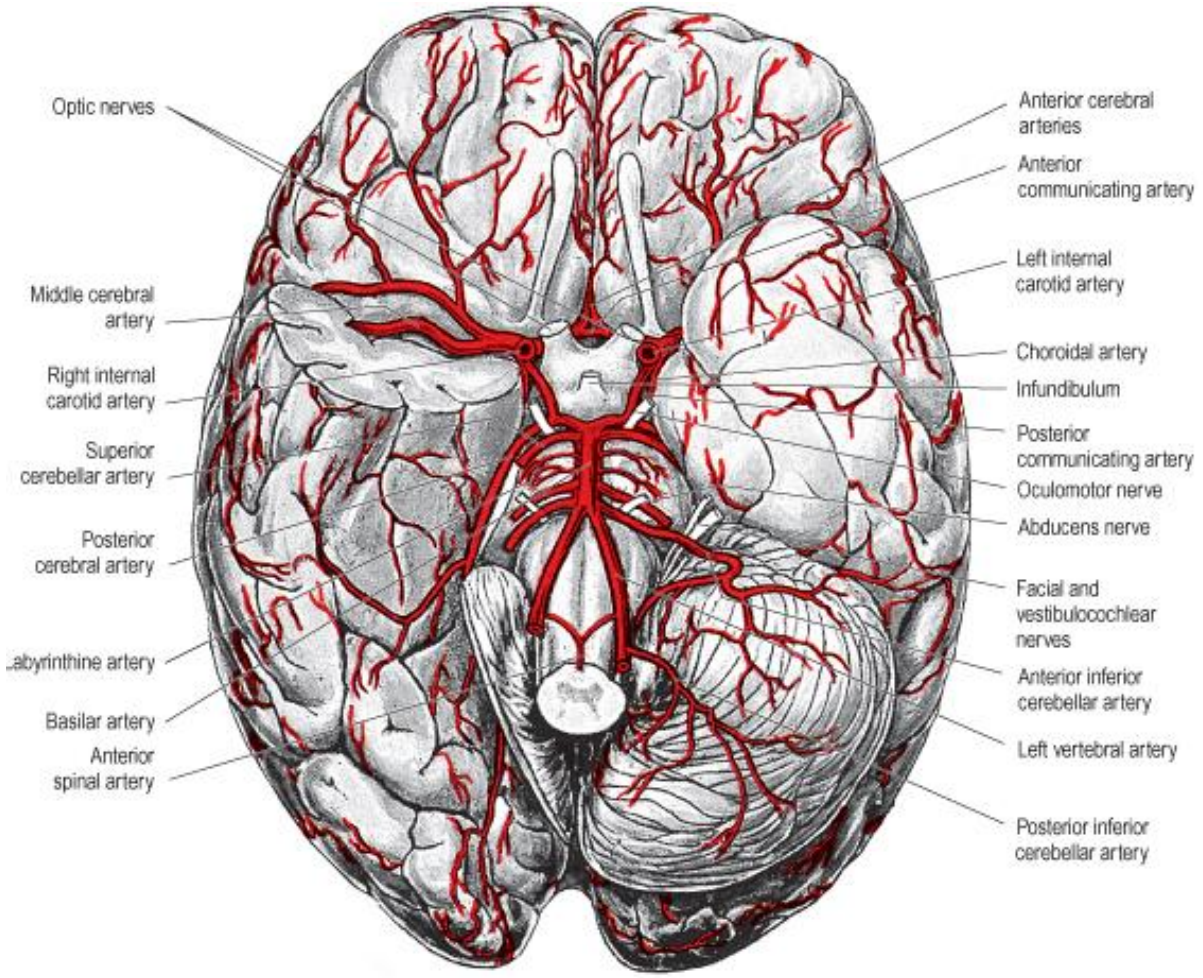
defence modality of prevention of stroke is identification & proper management of Risk factors.

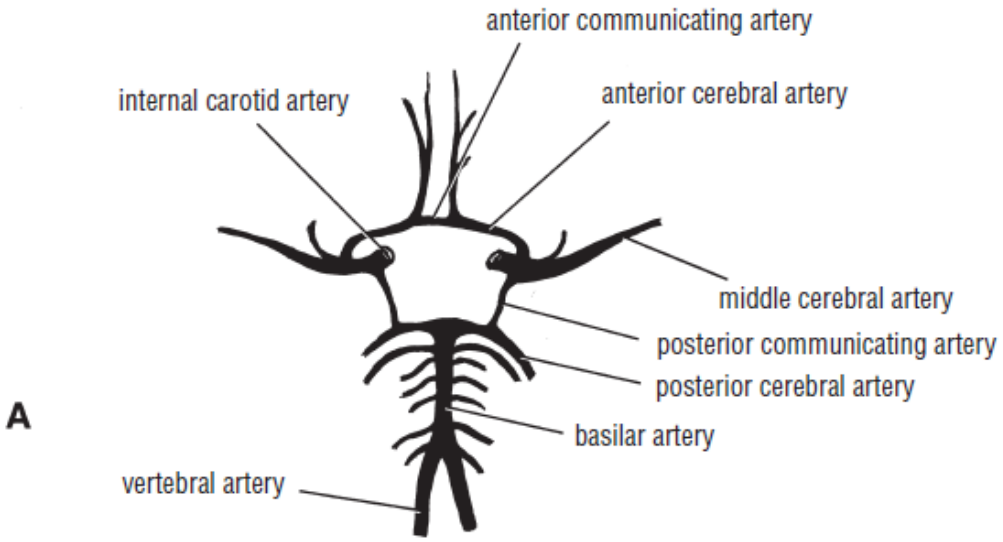
INCIDENCE AND PREVALENCE OF STROKE IN INDIA:

Stroke burden of a community is best reflected by the incidence. Two incidence studies conducted in late sixties and early seventies have been reported. There is only one well defined population based study from Vellore in South India by Abraham, Daniel (1972) and Sunder Rao (1973). This was conducted in two phases. In the first phase during 1968 -69, total urban and rural population of 258,576 was studied. The prevalence rate was more in Vellore town than in rural areas and the same increased with age. Subsequently, between 1969 & 71, the population was kept under surveillance and at the end of 2 years, prevalence and annual incidence rate of 84 and 13 respectively per 1,00,000 population was found.

The second study was earned out as a part of WHO collaborative study in Rohtak, Haryana between 1971 and 1974. The incidence was 27 per 100000. Though various prevalence studies were already done, prevalence by definition misses those who died or recovered from stroke. As the proportion of cases that either die or recover from stroke is more than 60%, the prevalence figures tend to underestimate the burden of disease by a fair margin. In one study overall range was 90 to 222 per 100,000 (TIA and death not accounted) Ischemic stroke from thrombosis and embolism constitute between 47.3% and 82.75% of all strokes. The incidence of hemorrhagic stroke was between 13.6% and 37.9% of all stroke cases. It is found that stroke is fairly common in young Indians < 40 years since they constitute 18.8 to 32% of all stroke cases.

ANATOMY OF CEREBRAL CIRCULATION





CIRCLE OF WILLIS

AREA OF BLOOD SUPPLY OF BRAIN

Figure 17.7 Major arteries of the brain. **A,** medial aspect; **B,** lateral aspect.

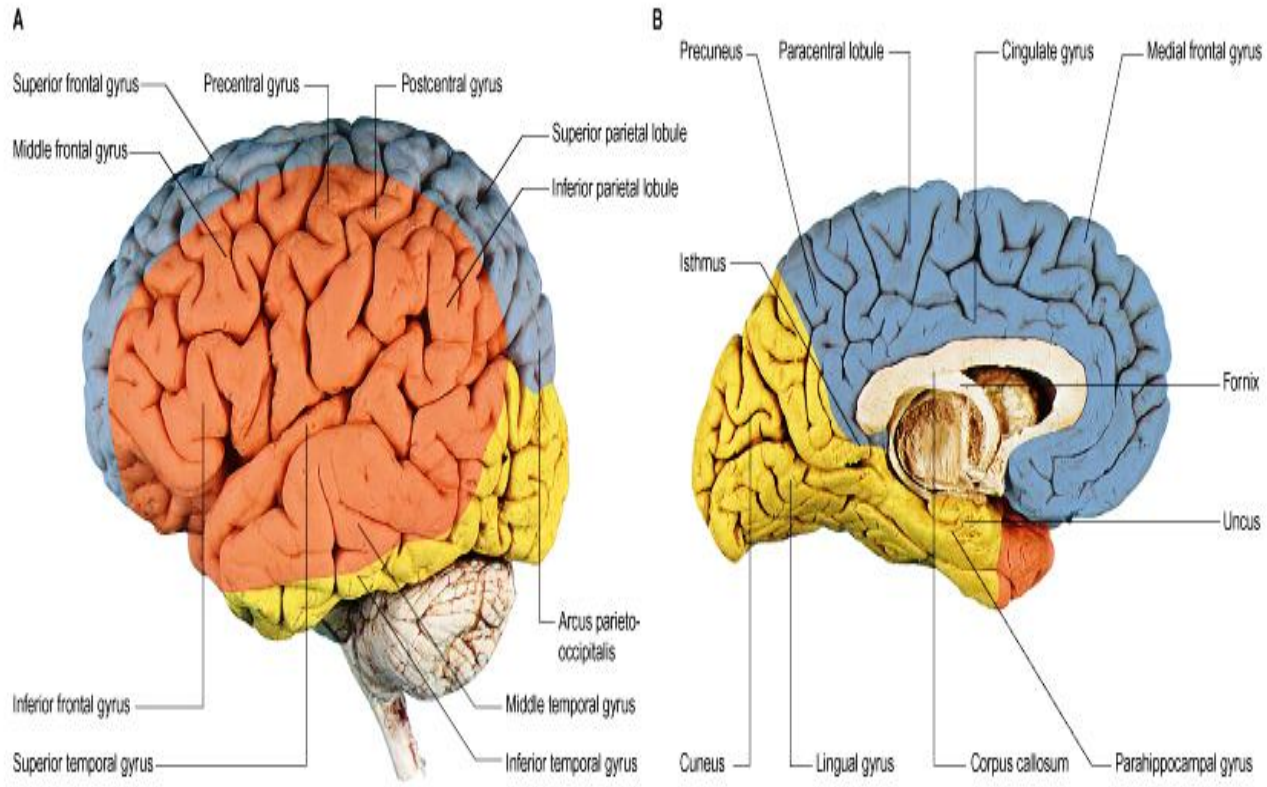
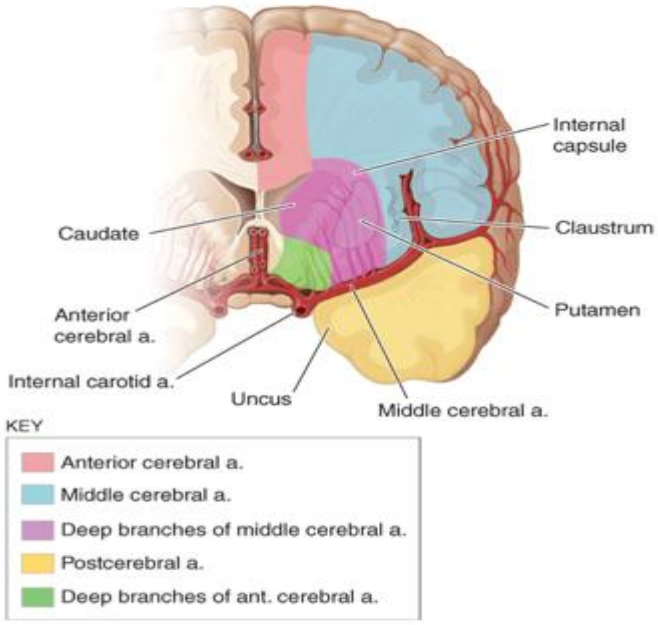


Figure 17.8 **A,** The lateral surface of the left cerebral hemisphere, showing the areas supplied by the cerebral arteries. **B,** The medial surface of the left cerebral hemisphere, showing the areas supplied by the cerebral arteries. In these figures the area supplied by the anterior cerebral artery is coloured blue, that by the middle cerebral artery pink and that by the posterior cerebral artery is yellow.



PHYSIOLOGY OF CEREBRAL CIRCULATION & CEREBRAL METABOLISM:

- The normal fuctions of brain are solely dependent upon a relatively constant supply of oxygen and glucose from the blood perfusing it(55-70 ml\100 gram of brain\minute).
- A fall in cerebral blood flow <8-9 ml\100 gram\minute results in ischaemia or infarction regardless of the duration. The state of hypoperfusion of the brain(CBF btn 8-23 ml/100gm/min) is called as "ISCHEMIC PENUMBRA".
- Conversely in the region of cerebral ischaemia, there is paralysis of "autoregulation" & the microvasculature is non reactive to pressure changes, the cerebral vasculature in this ischaemic zone becomes permeable to protein and fluid leaks in the vicinity("extracellular cerebral edema").Thus cerebral infarct is not the mere result of ischaemia from occluded blood vessels, but an end result of a series of highly complex modifying agents

CLASSIFICATION OF STROKE:

A) CLINICAL CLASSIFICATION:

1. **Completed stroke**: this is rapid in onset with persistent neurological deficit which does not progress beyond 96 hours. This term is applied to the temporal profile of the stroke syndrome in which the deficit is prolonged and often permanent, causing demonstrable parenchymatous changes

2.**Transient Ischemic Attack: c**haracterized by sudden focal cerebral or mono ocular function loss where symptoms last for < 24 hrs & It is also secondary to inadequate blood supply to cerebrum, ocular structures due to arterial thrombosis or embolism.

3. Reversible ischaemic neurological deficit:the deficit resolves without any residual deformity within a period of 1 to 3 weeks.

B). National institute for neurological disorders and stroke (NINDS).

NINDS has devised sub classification of ischemic stroke as per their pathology, clinical criteria & the vascular territory.

i. Clinical: cardioembolic, lacunar infarction. Atherothrombotic

ii. Mechanism:, Embolic, hemo-dynamic, Thrombotic

iii. Vascular territory: Internal Carotids, MCA (middle cerebral), ACA (anterior cerebral), Posterior cerebral, Vertebral or Basilar.

C). Oxfordshire stroke subtype classification

i. Primary intracerebral hemorrhage

ii. Total anterior circulation infarct constitutes 17% of all ischemic strokes.

iii. Partial anterior circulation infarct constitutes 24% of all ischemic strokes.

iv. Lacunar infarct constitutes 25% of all ischemic strokes.

v. Posterior circulation infarct constitutes 24% of all ischemic strokes

STROKE RISK :

Risk factors identification for stroke as well as awareness is of paramount importance as it helps in prevention of stroke. There will be slight difference in risk factors for infarction &haemorrhage.

The common risk factors are listed below.

Non-modifiable	**Modifiable**
Age	Hypertension
Sex	TIA
Race/ethnicity	Carotid artery disease
Genetics	Heart disease
	DMT2
	Smoking
	Dyslipidemia
	Obesity
	Ethanol
	Hyperfibrinogenemia, Homocysteinemia

1) **Blood pressure** : Hypertension is a major risk factor for stroke, whether hemorrhagic or not. About 40 percent of stroke is due to a SBP > 140 mm Hg.

2) **Smoking** : The Multiple Risk Factor Intervention Trial data showed smoking is directly having relation with stroke the same way it has to coronary heart disease. Framingham study showed threefold increase of ischemic strokes in smokers as compared to non-smokers. The effect was greater at younger ages and paralleled the number of cigarettes smoked.

3) **Obesity**: BMI is predictive of stroke among smokers & non smokers. BMI > 25 kg/m^2 and smoking is responsible for sixty percent strokes in men until 65 yrs of age.

4) **Diabetes Mellitus**: Another widely accepted risk factor for stroke as a whole, and particularly for ischemic brain infarct, is diabetes mellitus. In the Framingham study it was the sixth most important predictive factor for stroke.

5) **Transient Ischemic Attacks** : By and large one might expect that after 2-4 years, one out of six patients with TIA would have suffered a thrombotic stroke.

6) **Cardiovascular Disease** : Electrocardiographic changes of left ventricular hypertrophy raises risk of ischemic event by ten times, nonspecific ST23 changes by four times and Cardiac failure by nine fold according to the Framingham study.

Hypertension and peripheral vascular disease, myocardial infarction, cardiac arrhythmias, valvular and congenital heart diseases are the predisposing factors of embolic type of stroke. Those with chronic fibrillating atrium are 5 to 7 times more liable to embolic stroke than age matched population with normal cardiac rhythm. Mitral valve prolapse, valve prosthesis, Endocarditis, congenital heart disease are all important causative factors for embolic stroke.

PATHOPHYSIOLOGY OF STROKE

From the stand point there are two processes:

1) Ischemia, & infarction due to decrease or loss of vascular supply results in loss of oxygenation to brain.

2) Disruption of Cerebral vessels leads to hemorrhage

IN ACUTE ISCHEMIC STROKE

The pathophysiology of cerebral damage from vascular occlusion has two steps:

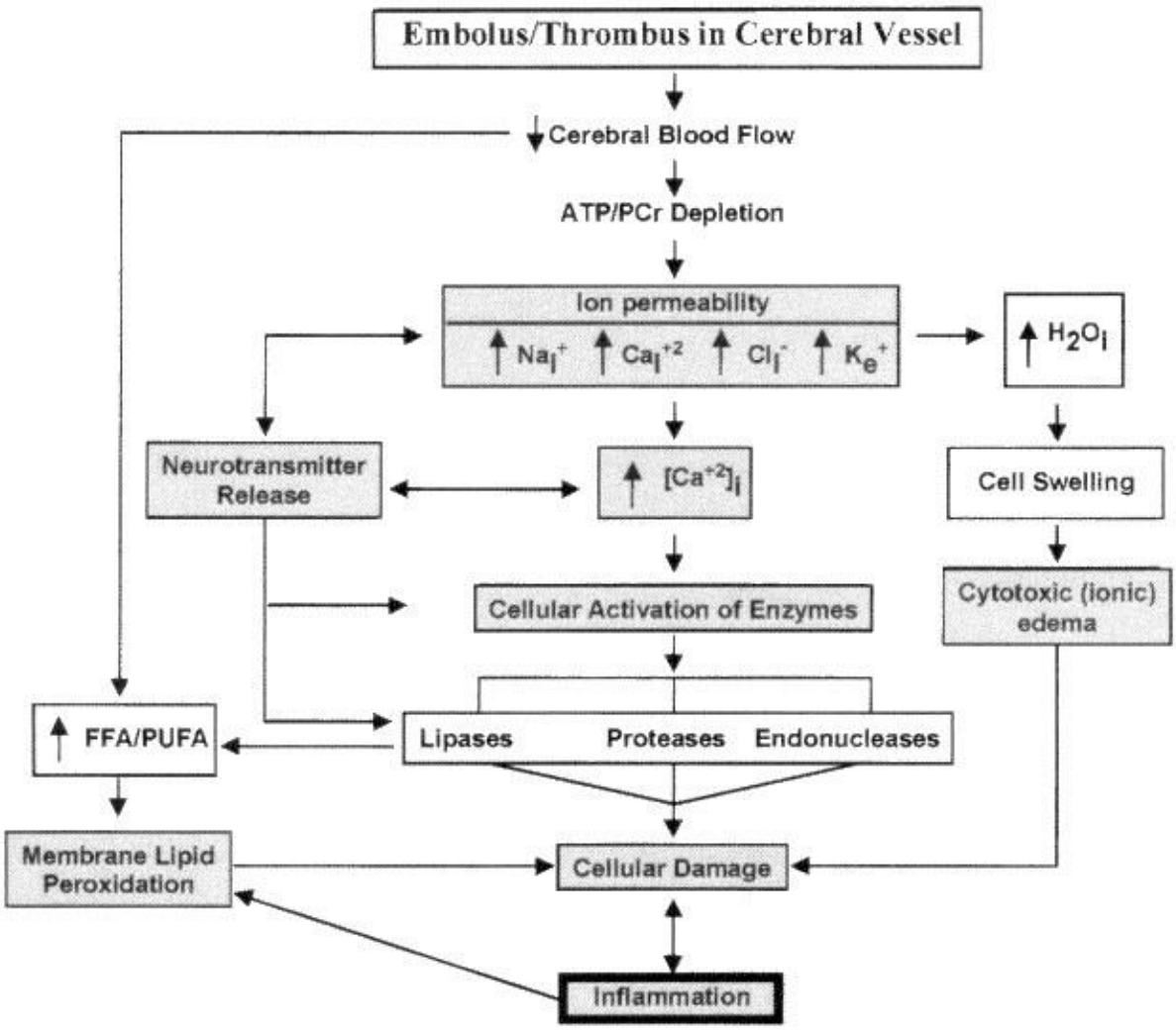
1) Haematological &Vascular events that results in reduction initially and

further alteration of local blood flow to brain.

B) Ischemia induced changes at cellular level mechanics causes death of

neuronal cells, glial tissue & supportive cerebral cells.

The molecular level changes due to cerebral ischemia are changes that happen in cellular signalling, transduction of signal, metabolism & gene regulation / expression.



All shaded boxes shows major changes that happen in ischemic stroke. Energy availability decreases in stroke, so membrane ionic primes fail.

The raise in ECF potassium reaches levels adequate to release

neurotransmitters like glutamate & aspartate that are excitotoxic & also stimulates Na/Ca channels coupled to glutamate receptors that can help in development of cytotoxic edema. The influx of Ca through Ca channels raises free cytosolic calcium which is responsible for mitochondrial Ca overload. ATP production ceases & extensive cellular proteins, nucleic acids phospholipids breakdown due to Ca2+ mediated activation of proteases, endonucleases & phospholipases. Free radicals formed in this processes contributes to lipid peroxidation, nuclear DNA and protein toxic changes & cellular damage (a.k.a apoptosis/ necrosis).

When blood flow to cerebrum is around 10-15 ml / 100 gram/ ml, it deprives neuronal tissue of substrates & O2 needed for oxidative processes. In minutes once ischemia sets, demand is more than the brain's ATP synthesising capacity anaerobically from its meagre glycogen stores. Hence high energy phosphates & substrates for their production are depleted. Lactate accumulates at the beginning of ischemia. H+ ions toxicity and its ability to facilitate free radicals can cause injury to astroglial tissue.

Energy dependent mechanisms when they fail causes worsening of ion

Gradients in membrane, opening of ion channels & equilibrium state of most Intra & extra-cellular ions leads to Anoxic depolarization. Hence K+ ions leave the cell, Na, Cl & calcium ions enter cells. Various neurotransmitters are effluxed in concentrations that are toxic. There is Calcium mediated activation of phospholipases, in turn it hydrolyzes glycero-phospholipids to free fatty acids & this in turn facilitates free radical peroxidation of other membrane lipids. It catalyses activation of proteases that lyses structural proteins and activates nitric oxide synthase to begin free radical mechanisms.

Pathogenesis of moderate ischemia includes several compensatory mechanisms, which plays a role in maintaining normal concentrations of Adenosine Tri phosphate, membrane ion gradients & viability of cell.

50% reduction of Blood flow to brain decreases electro-encephalographic activity, and only slightly higher ischemia completely blocks synaptic level transmission which leads to an isometric electro- encephalogram.

The slight increase in membrane K+ion conductance can hyperpolarize pre & post-synaptic membranes, hence decreasing release of neurotransmitters & the postsynaptic receptors responsiveness to neuro-transmitters. Various

mechanisms that are responsible for an increased K+ ion conductance involves modulations in ATP regulated and Ca regulated channels.

In spite of these compensatory pathways that compromise physiological activity to decrease energy utilization thereby preserving viability of cells, cell necrosis happens when moderate ischemia extends for few hours.

Calcium ion homeostasis dysregulation features mainly in the lethal effect in cells of both moderately and severely ischemic brain. In moderate ischemia there is the partial conservation of energy dependent mechanism which regulates calcium ion concentrations inside the cell. This is different from the depletion of ATP and the complete loss of calcium homeostasis in severe ischemia. Hence blockade of channels in the membrane permeable to calcium pharmacologically may decrease calcium within cells to less than toxic levels in moderate ischemia alone.

Of the many causes of ischemic strokes, thrombosis – complicating atherosclerosis of intra and extra cranial vessels ultimately accounts for most of the cases. The damage that atherosclerotic thrombosis causes to the brain is determined by the available collateral circulation, the speed of thrombotic

occlusion and by embolism distal to the thrombus. There is a tendency for atheromatous plaques to form at branching and curves of the cerebral arteries.

The most frequent sites are:

i. Internal carotid artery at its origin from the common carotid

ii. Cervical part of vertebral arteries and at their junction to form basilar artery.

iii. In the stem or at the main bifurcation of the middle cerebral arteries.

iv. In the posterior cerebral arteries as they wind around the midbrain.

v. In the anterior cerebral arteries as they pass anteriorly and curve over corpus callosum.

PATHOPHYSIOLOGY OF THROMBOTIC STROKE

The process of thrombus formation involves interplay between three components, the endothelium, circulating platelets and a series of biochemical events that constitute a 'coagulative cascade'.

When atherosclerosis is the primary condition, thrombus formation usually begins with a localized injury to the endothelium. The endothelium overlying a plaque suffers from damage from hemorrhage or necrosis of vessel wall secondary to an alteration of the vasovasorum. Thrombus forms fibrin and

platelet adhere to the endothelial surface and leads to partial or complete occlusion of the lumen. In the process aggregates of platelets are attracted to the site, partly through the action of prostacyclin. Vasomodulin on the surface of the endothelium with protein C, which normally inhibits the formation of fibrin through its interaction with thrombin is reduced at the injured site and induces clotting. Homocystine has similar effect and is believed thereby to promote thrombosis. Circulating platelets increase in number locally, enlarge, and become more adherent to one another and to the injured vessel. As they aggregate they discharge their granules. This process is stimulated by thromboxane A2, which is synthesized in the injured vessel wall. The third component coagulation cascade involves the interplay of series of factors that result in the formation of thrombin and the conversion of fibrinogen to fibrin. Involved in this process are changes in a number of natural anticoagulative products like heparin cofactor2, anti-thrombin iii, protein C & protein S. A deficiency of any of these factors may predispose to in-situ thrombosis within either the arterial or venous systems.

The middle cerebral artery stem, the major vessels forming the

Circle of Willis ,the basilar , the vertebral arteries gives up to 100 to 300 micrometer diameter branches which penetrates deep white and grey matter. These vessels may be thrombosed by athero-thrombotic mecahnisms at its origin or by lipo-hyalinotic thickening mediated infarcts referred to as LACUNES. They range in size from as small as 3 to 4 mm to 1 to 2 cm.

Embolism is one of the common causes of ischemic stroke. Heart is the common source of emboli. Among the cardiac causes, rheumatic valvular heart disease with atrial fibrillation is the commonest cause. Myocardial infarction can cause embolism. Tiny septic emboli form multiple abscesses in brain in infective endocarditis. Paradoxical embolism from systemic circulation occurs in congenital heart disease with shunt or even in patent foramen ovale. Post surgery embolization is a high risk in intracardiac surgery and prosthetic valve replacement. Atrial myxoma results in tumor emboli. Mitral valve prolapse and mural thrombus can cause embolization.

EVALUATION OF PATIENT WITH STROKE:

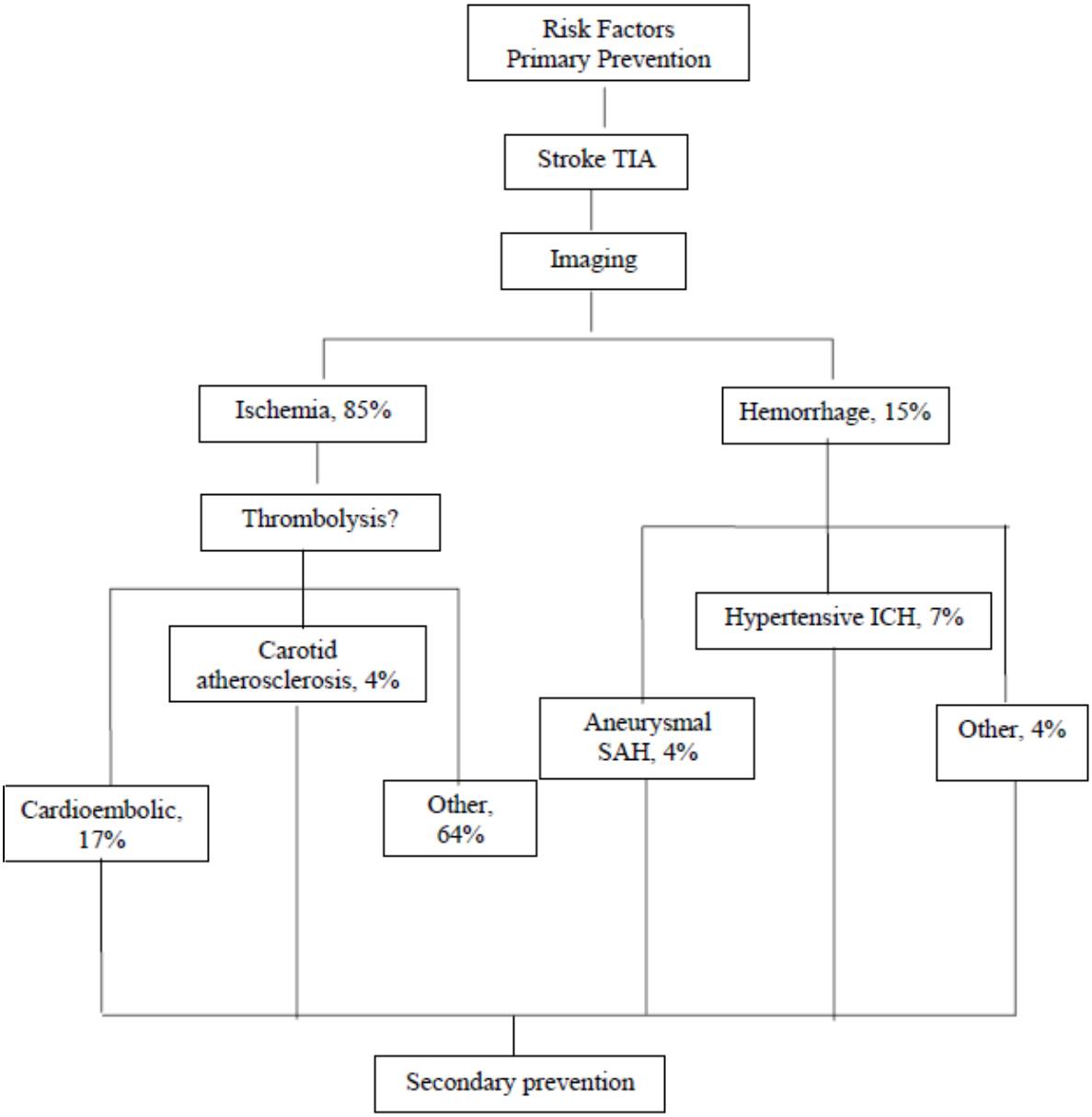
Of all those who have stroke only about one third of them are aware of the symptoms. When these symptoms are identified, assessment must start with Evaluating the patients' ABC's of resuscitation. Ventilation, circulation abnormalities that need immediate interventions are generally rare at the time of stroke.

In hospital adequate triage is essential. The general assessment includes an adequate history, examination, Spo2 monitoring; glucose, electrolytes, Full blood count, coagulation tests, ECG and CXR.

The neurologic examination should include assessment of dysphasia, hemiparesis or sensory loss, hemianopia and other signs of focal deficits. Any focal deficit if present which has an abrupt onset in the absence of trauma indicates stroke.

But further evaluation is carried out in the form of imaging studies, for (a) precise localization of ischemia or haemorrhage and (b) to ruling out other mimickers of stroke like seizures, hypoglycaemia, tumor, migraine & HTN encephalopathy.

.Evaluation:



Schematic approach to acute stroke [5]. Numbers are percentage of all strokes. Abbreviations TIA,(transient ischemic attack), SAH,(subarachnoid hemorrhage), ICH,(intracerebral hemorrhage).

CLINICAL FEATURES OF ACUTE STROKE

1)Athero thrombotic stroke

Ischemic type of stroke can be thrombotic or embolic in etiology. The main etiological factors are Systemic hypertension & atherosclerosis. SBP (systolic) is as important a risk factor as DBP (Diastolic pressure). DM, dyslipidemia are other risk factors.

Most of the times there is a preceding episode of Transient ischemic attacks lasting for a period of < 10 min which indicates thrombus of the major vessels that is evolving. In embolism there are numerous episodes of TIAs extending for several hrs causing complete deficit. Twenty percent of infarcts that succeed Transient ischemic attacks happen less than one month after the initial attack while fifty percent% happens in one year.

Transient ischemic attacks can be for a few seconds or up to twelve to fifteen hrs; mostly they last from two to 15 mins. Between attacks, there may be no neurological deficits. In most of the patients, attacks has no relation to activity or position, though they are likely to occur when the patient is mobile

than when they are resting. Main pathology is closely associated with vessel stenosis, atherosclerotic ulceration & thrombotic plaque formation.

Though TIA's refers to any abrupt onset focal neurologic deficit which disappears completely in < 24 hrs, this term is very broad as it does include other entities that are not always due to ischemia per se like an epilepsy or a migraine with CNS symptoms. Hence it is best to consider focal and completely reversible, ischemic episodes extending from minutes to an hour as Transient ischemic attack. Ischemic signs extending > 24 hrs and < than seven days is known as RIND (reversible ischemic neurologic deficit).

Stroke in Evolution - indicates neurological deficit which progress or has fluctuating course when the patient is in observation, where as 'completed stroke' means there is no further deterioration. Such Fluctuation in the neurological status are mostly due to thrombus or emboli moving, breaking & disappearing from one vessel to another, and are caused by repeated artery to artery embolization / collateral flow which fluctuates.

It develops mainly in one of the following ways:

1. stroke in evolution - There could be a single attack evolving in a few hours
2. stroke in evolution - “stuttering” progression extends over several hrs or longer than a day.
3. A partial stroke which occurs but recedes temporarily for few hrs after which there is rapid worsening to completed stroke.
4. More confusing one is a “slow stroke” which evolves over weeks and is secondary to long term hypo-perfusion.

Occurrence of stroke during sleeping hours or immediately after getting up is another feature of thrombotic type of stroke. At the beginning symptoms like vomiting, headache, and LOC are less frequent than with intracerebral hemorrhage. The headache in ICH/SAH is more violent associated with neck stiffness. Based on specific territories of cerebral supply involved a number of syndromes are described. MCA involvement is the most common that results in complete or partial motor hemideficit, hemi-anaesthesia, hemainopia(homonymous type) and language deficits.

2) Lacunar infarcts

It constitutes ten to fifteen percent of all types of strokes. They are due to infarcts in the deeper parts of the cerebrum secondary to lipohyalinosis or microatheromas in the deep penetrating vessels giving supply to internal capsule, basal ganglia, & paramedian region of brainstem. These are very small and not seen in 1/3rd of the subjects. Types are pure motor , pure sensory stroke, Clumsy Hand dysarthria syndrome, ataxic hemiparesis and pseudobulbar syndrome. Death is uncommon.

3) Embolic infarction

Most of the times, embolic source is cardiac in origin which could be due to (AF) atrial-fibrillation Rheumatic or valvular or atherogenic cardiac illness, MVP. Major sites are obstruction in the MCA, at the upper division and the PCA, at the bifurcations.ACA occlusion is uncommon.

Stroke can cause a severe deficit that improves rapidly due to dissolution of the embolus. It is the most important reason for a single evanescent event.

Sustained CNS deficits depend upon the regions involved. Emboli that are

small can occlude the MCA branches producing focal disorders like - Receptive aphasia, motor aphasia, monoplegia. It is thought of in younger individuals where consciousness is well present even after higher grade of neurological deficits.

INVESTIGATIONS:

Computerised Tomography:

It is one of the important investigations in Stroke patients.

→Rapid, less expensive & easily available.

→Drawback is low sensitivity.

Middle cerebral artery region infarct identification is around 70% in the first six hrs , though changes in the deep grey matter nuclei like lentiform is identifiable in < 1 hr of occlusion in around sixty percent of subjects.

The main role of Computerised Tomography in emergency setup:

1. Rule out ICH, important to avoid unnecessary thrombo-lysis
2. Identify early subtle signs of infarction
3. Rule out other cerebral tumours which mimicks stroke

The first sign identified is a hyperdense segment of an artery, reflects vessel thrombosis or emboli. It is well seen in MCA (Middle Cerebral Artery Hyperdense sign).

Hyper-acute stage (1-3 hrs)

In the initial hrs depending on the site of block and collateral flow a few signs are noted. These include:

→Loss of differentiation of grey & white matter, and reduced attenuation of the deeper nuclei - lentiform nucleus, seen in seventy five percent pts at three hrs

→ Loss of insular ribbon sign.

One week

Significant mass effect causes 2^{o} damages in those with larger infarcts.

2-3 weeks

Petechial haemorrhages with the cortex seen

Months

Gliosis establishes & seen as a low density region.

Computerised Tomography guided Angio:

1. Identification of intracranial vessel thrombus thus guiding clot retrieval or

thrombolysis.

2. Establishing etiology and assessing limitations in endo-vascular

treatment.

MRI

MRI is more time consuming and less available than CT, but has significantly higher sensitivity and specificity in the diagnosis of acute ischaemic infarction in the first few hours after onset.

T-1 IMAGE

→Low intensity signals roughly mirrors high T2 / FLAIR signal

→High intrinsic T1 signal due to laminar cortical necrosis seen as a ribbon mostly > two weeks

DWI

Diffusion restriction is usually seen within minutes once ischemia sets in and it depicts the Infarct site well

T2-weighted imaging and FLAIR

Low sensitivity compared to Diffusion Weighted images in the initial hours

Initially there is loss of normal signal void in large arteries.Within six to twelve

hrs, there is high signal within the infarcted tissues Effacement of sulci & mass effect establishes- it gets maximal in the intial period.

Fogging: between 1 - 4 weeks inflammatory cells infiltrates can decrease T2 signal & it gets relatively iso-intense to brain parenchyma that is normal.

GRE/SWI

High sensitivity for haemorrhagic stroke

TREATMENT: After the diagnosis of stroke is made, the main aim is treatment for prevention or reversal of brain injury. Includes the following

(a) Medical management

- Control blood pressure (if more than 185/110mmHg)

- Maintain serum glucose at < 200mg/dl

- Anti oedema measures to reduce ICP

- Preventing infections, deep vein thrombosis (DVT), and bedsores.

(b) Thrombolysis-intravenous or intra arterial 19

(c) Anticoagulation- for stroke in evolution

(d) Neuroprotection

(e) Rehabilitation

In Intracerebral hemorrhage

(a) Supportive treatment (as in ischemic stroke).

(b) Surgical evaluation (for cerebellar hemorrhage)

PRIMARY AND SECONDARY PREVENTION OF STROKE:

GENERAL PRINCIPLES:

A number of medical and surgical interventions, as well as life-style modifications, are available for preventing stroke. Some of these can be widely applied because of their low cost and minimal risk; others are expensive and carry substantial risk, but may be valuable for selected high-risk patients.

Hypertension is the most significant of the risk factors; in general, all Hypertension should be treated. The presence of known cerebrovascular disease is not a contraindication to treatment aimed at achieving normotension. Also, the value of treating systolic hypertension in older patients has been clearly established. Over control of Blood pressure must be avoided, however; the treatment goal is to achieve normotension gradually.

Treatment of hypercholesterolemia with statin drugs were found to lower stroke risk. As CAD is most important cause of mortality in those with CVD,

treatment of hypercholesterolemia seems prudent for both the heart and brain. Tobacco smoking should be discouraged in all patients. Whether or not tight control of blood sugar in patients with diabetes lowers stroke risk is uncertain.

ANTIPLATELET AGENTS: act by inhibition of intraarterial platelet aggregate formation. Clopidogrel, Aspirin and dipyridamole are the antiplatelet agents used most for this purpose.

ANTICOAGULATION THERAPY:

There are few data to support the use of long-term warfarin for preventing atherothrombotic stroke, either intracranially or extracranially. Several large trials are in progress.

Thromboembolism is one of the most serious complications of prosthetic heart valve implantation. Anticoagulation has been proven to be effective for preventing strokes in this situation and a greater degree of anticoagulation (INR of 3 to 4, depending on valve type) is recommended for prosthetic heart valve patients. If source of emboli is not cleared, anticoagulation must be given life time. Secondary prophylaxis for ischemic stroke of unknown origin is controversial. Some physicians prescribe anticoagulation for 3 to 6 months

followed by antiplatelet treatment.

SURGICAL THERAPY:

Surgery is mainly for plaques at the origin of the ICA -internal carotid artery in the form of Endarterectomy.

Symptomatic carotid stenosis was studied in the North American Endarterectomy trial Collaborators (NASCET) and the European Carotid Surgery Trial (ECST). It showed that there was a substantial use in patients with a stenosis of >70%. In NASCET, the average ipsilateral stroke rate at two years was found to be 26% for patients treated medically and 9% for those receiving the same medical treatment plus a carotid endarterectomy. This 17% absolute reduction in the surgical group is a 65% relative risk reduction favouring surgery. NASCET also showed a significant benefit for patients with 50 to 70% stenosis, although less robust. ECST found harm for patients with stenosis in the 0 to 30% range treated surgically.

The indications for surgical treatment of asymptomatic carotid disease have been clarified by the results of the Asymptomatic Carotid Atherosclerosis Study (ACAS), which randomized patients with 60% stenosis to medical

treatment with aspirin or the same medical treatment plus carotid endarterectomy. The natural history of asymptomatic stenosis is an approximate 2% per year stroke rate, whereas those patients with symptoms have a 14% per year stroke risk. To advise Surgery for a patient without symptoms is always in dispute & decided by other factors including patient age, preference, co-morbidities. Medical therapy for reduction of atherosclerosis risk factors and aspirin, 325 mg/d, are generally recommended for patients with asymptomatic carotid stenosis. As with atrial fibrillation, it is imperative to counsel the patient about TIAs so their therapy can be revised if they become symptomatic.

CRP (C – Reactive Protein)

It was the first protein to be discovered which behaves as an acute phase reactant. It has been named for its calcium-dependent interaction with the somatic C-polysaccharide of pneumococci (CPS).

C-Reactive Protein was discovered by Tillet and Francis in 1930, when they investigated immunological reactions with extracts of Streptococci in

Pneumonia. It was found out that the serum of acutely sick patient was precipitated by a fraction ‘C’ (non type-specific somatic polysaccharide). Once the event resolves, the ability of the subjects serum to precipitate CPS is lost and the C-Reaction material was not found in the serum of normal individuals.

Avery et al (1941) identified that the CRP is a protein that requires Ca ions for its reactions with C-polysaccharide and gave the term “acute phase” to represent serum drawn from acutely ill patients having infectious disease .

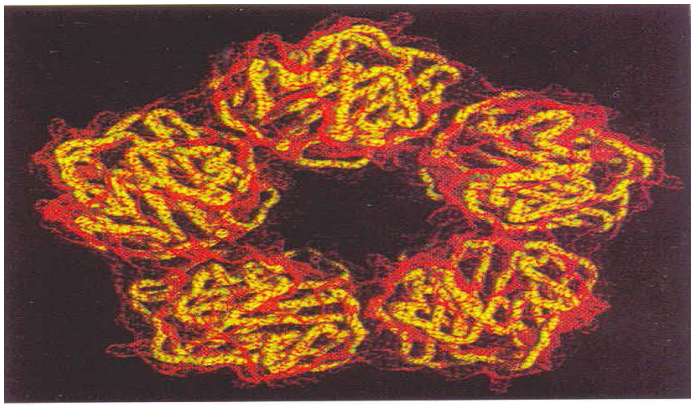
Lofstrom, (1944) identified a Quellung reaction of few strains of pneumococci and also noted that the factor responsible for it was C-Reactive Protein. He identified CRP raise in infectious & non-infectious conditions. In atherosclerotic plaque inflammation is very important and it is related with macrophages, endothelial cells and smooth muscle cells activation & proliferation.

Literature Review insist on the fact that cerebro-vascular events do happen amongst those without evidence of very high cholesterol levels and there is a need for good risk stratification methods.

Of all risk factors know at present, hs- C-Reactive Protein, a marker of

low grade vascular inflammation, is among the most promising. Various studies do show us that hs-C-Reactive Protein adds as a valuable prognostic tool for all LDL cholesterol levels and at all stages of the Framingham risk score.

CRP is associated with Metabolic Syndrome and onset of DM. Evidence does show us that C-Reactive Protein independently identifies cerebral thrombotic episodes. It also is a good predictor of risk of stroke independent of the Framingham co-variates. After adjustment for BP, DM, dyslipidmeia, smoking, the risk of recurrent stroke in Framingham heart study raised by 25% in men and 29% in women for each increasing value of CRP. Hence CRP act as an important means of predicting risk in addition to the one achieved by simple measurement of burden of atheroscelrosis.



Pentameric structure of CRP

Synthesised in Liver hepatocytes and the increased release is driven by cytokines from macrophages (activated). The concentration of C-Reactive Protein can rise upto 10000 fold.CRP levels is proportionately related to the presence & severity of cardiac, cerbrovascular and peripheral vascular atheromas.

Tumour necrosis factor, interleukin-1 and interleukin-6 also mediate acute phase response.61 These soluble mediators react with hepatocytes and can influence the expression of specific genes in hepatocytes which are responsible for synthesis of certain proteins that are part of the acute inflammatory response. These includes all acute phase reactants like CRP, A-1 antiproteinase, hapatoglobin, C3 and fibrinogen. CRP is the earliest one to increase in inflammation. It is a protein that reacts with capsular polysaccharide of *streptococcus pneumonia* and can activate complement by classical pathways.

Today, however, the best single test of acute inflammation is C-Reactive Protein level that can be readily quantified by nephelometry.

INFLAMMATORY STIMULI

↓

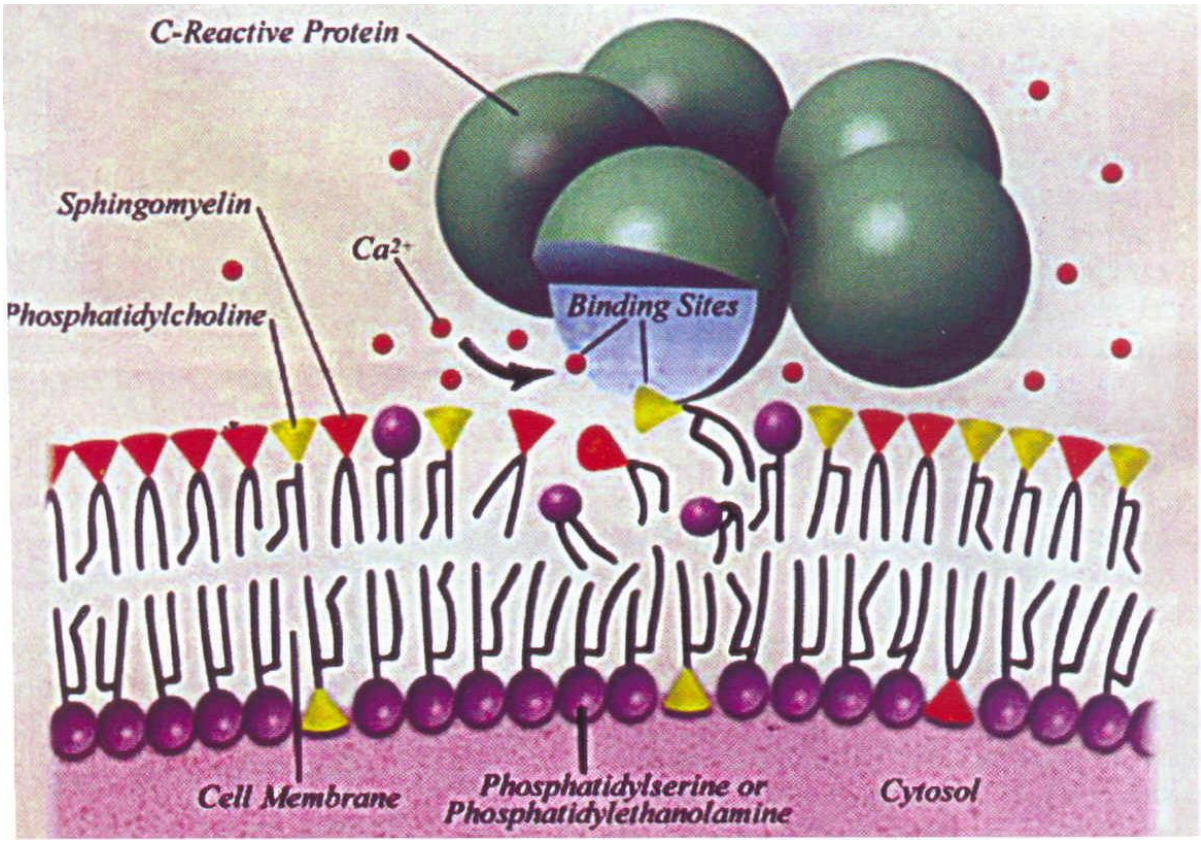
IL-1, IL-6, Tumour necrosis factor → C-Reactive Protein

↓

MD – monocyte derived macrophage, endothelial cellactivation, Tissue factor, and adhesion molecules etc.

↓

Atherosclerosis



Complexion of CRP to cell membrane

C-Reactive Protein has profound pro-inflammatory property. It can also Promote the synthesis of monocyte chemotactic protein-1 (MCP-1) thereby activating recruitment cascade.

The average circulating levels is 0.8 mg/l.

90%	<3 mg/l
99%	<10mg/l

The rate of synthesis and secretion of C-Reactive Protein increases in few hours of an acute injury, due to various humoral mediators such as endogenous leukocyte mediator a Pyrogen66 and PGE (prostaglandin). It may reach peak values upto 300 mg/ml in less than 1-2 days. It is a part of Pentraxin family of proteins with a mol. weight of 105500 Da. It consists of non glycosylated identical positive polypeptide units, associated non covalently in a disc configuration, forming a pentameric (cyclic) symmetry. The structure & the sequence of the amino acid subunit are different from other known proteins except amyloid P.

FUNCTIONAL PROPERTIES OF C-REACTIVE PROTEIN

C-Reactive Protein causes precipitation of soluble ligand and agglutination of Particulate ligand through its calcium dependent or its polycations binding venues, it is a strong activator of the complement pathway (Classical) beginning in C1q. Through Complement activation, there happens adherence reactions and fixation of C5b-C9 complexes and in the end lysis when the ligand is on cell surface.

Complement split fragments, which gets activated in the fluid phase are formed. C-Reactive Protein like Anti-bodies can attach to the ligands, carry out opsonisation, phagocytosis & begin cell damage. Of all the hypothesis given now it is known that atherosclerosis is an inflammatory process and that C Reactive Protein has a profound pro-inflammatory effect. Using MCP-1 activation as an assay, Edward T.H. Yeh, showed that both lipid lowering agents can block C-Reactive Protein mediated MCP-1 stimulation.

Additional Role of CRP includes:

1. T-lymphocytes selective binding and modifying its functions.

2. Platelet Aggregation & activation suppresion.

3. Phagocytes activity and mobility enhancement.

C-Reactive Protein was found out in the lesion which was associated with C3 deposition, angiotensin-1-receptor [ATI-R], vascular CAM-1 and expression of collagen. These enlighten us that C - reactive protein in vivo has a Pro- atherogenic role.

However, the most important role played by C - reactive protein is to recognize the toxic autogenous materials from dead & damaged tissues in plasma, to facilitate their clearance by binding & detoxifying them.

CLINICAL IMPLICATIONS IN CRP MEASUREMENT:

->Absence of circadian variation

->Diet doesn't alter its levels (patient need not fast)

Measuring the levels of cholesterol & C - reactive protein enhances the predictive value of C-Reactive Protein. When both are high overall risk of CVA rises up to 9 times on comparing to those with decreased C-Reactive Protein & cholesterol.

CRP synthesis is not altered by any therapies, unless these affect the underlying disease processes that provoke the acute phase reaction. The only scenario that alters the normal C-Reactive Protein levels is liver failure.

DETECTION AND MANAGEMENT OF INTERCURRENT INFECTION

Increased level is a useful indicator of possibility of infection in otherwise normal subjects or individuals with a primary condition that predisposes to infection. adequate therapy of the infection source leads to a prompt fall in CRP levels on the other hand if the levels remains the same it shows continuing activity of the underlying disease process.

CONDITIONS ASSOCIATED WITH MAJOR RISE OF CRP

→Allergic complications of infection, Erythema nodosum leprosum

→Rheumatic fever

→IBD

→PMR (Polymyalgia Rheumatica)

→Rheumatoid and Psoriatic arthritis

→Ankylosing spondylitis,

→FMF

→Graft rejection, Post transplantation.

→Malignancy- sarcoma, lymphoma,

→Necrosis Myocardial infarction, tumour Embolization

→Pancreatitis

→Burns, Traumatic fractures

EPIDEMIOLOGICAL STUDIES

Curb et al. had done a study based on serial review of C-Reactive Protein measured from 259 thromboembolic stroke cases and by comparing it with 1348 people as control population. It showed positive association of CRP with thrombotic and embolic stroke.

Weinbeck et al. studied 127 patients with first ischemic stroke and compared C-Reactive Protein levels at admission, 24 hours and 48 hours. They found that C-Reactive Protein levels at 12 and 24 hours are independent predictors of unfavourable outcome.

Muir et al. studied 228 ischemic stroke admissions. Median follow up was 959 days. Geometric mean C-Reactive Protein concentration was > 10.1 mg/L. It was found that survival in those with C-Reactive Protein> 10 mg/L was significantly worse than in those with C-Reactive Protein < 10 mg/L (p 0.0009, log rank test). They concluded that C-Reactive Protein concentration is an independent predictor of survival after ischemic stroke. The single independent predictor of survival in this study was measurement of CRP within 72 hours of onset of symptoms.

Natalia et al. prospectively studied 591 men and 871 women from 1980-82, when 196 ischemic strokes and TIAs occurred. They concluded that elevated plasma C-Reactive Protein levels significantly predict the risk of future ischemic stroke and TIAs in the elderly without being dependent on other cardiac risk factors.

Di-Napoli et al assessed the relation between blood pressure and basal concentrations of C-Reactive Protein in the first 24 hours after onset of stroke. The associations were calculated based on regression methods. They found that for each 10 mmHg raise in SBP, DBP, MAP and the odds of a greater value of CRP raised as well by 72% , 10% , 21% and 10% (significant p value) respectively. Thus higher SBP is definitely having a significant association with increasing levels of CRP in patients of ischemic stroke.

THE ERYTHROCYTE SEDIMENTATION RATE (ESR)

→Otherwise known as **Westergren ESR**, is the rate at which there is sedimentation of RBC's within 1 hr. It is another inflammatory marker. It utilises blood that is anti-coagulated and kept in a vertical tube named Westergren's tube and measures the rate of fall of RBC then reported as millimetre/hour.

→ESR is an indirect measure of inflammatory response in contrast to CRP

→Red blood cells do not clump together due to their negative charge which repel each other normally

→Positively charged plasma proteins neutralize the negative charge of RBCs, resulting in them stacking as roleaux or tyres.

→Roleaux has a greater surface to mass ratio compared to a single RBC hence faster sedimentation

It is also a very good means of measuring morphology of RBC as well as that of plasma protein composition and concentration. Concomitantly there is a raise in levels of C-Reactive protein.

Alteration in surface area of RBC and its density changes ESR. It makes roleaux formation difficult and hence a disproportionately low erythrocyte sedimation rate as in sickle cell disease & hereditary spherocytosis.

Doubts if any discrepancy must be corrected by assessment of the various

determinant factors of Erythrocyte Sedimation Rate.

In 1897 it was first found and used by Edmund biernacki a pathologist.

Hence it is also called as BIERNACKI's Reaction.

Advantages : many a times helps in diagnosing diseases like

-> Multiple Myeloma

-> Polymyalgia Rheumatica

-> Autoimmune Diseases

-> SLE, RA, IBD, CKD where its values can be > 100 millimetre/ first hour.

-> Koch's disease, cardiac illness.

-> Infective endocarditis

Stages in erythrocyte sedimentation:

a) First stage - 10 min - Rouleaux formation

b) Second stage - 40 minutes – settling/ sedimentation

c) Third stage -10 min – packing stage settling slows and cells pack in the bottom of the test tube.

Reference Values: millimetres per hr

AGE	20	55
Males	12	14
Females	18	21

ESR is an easy and affordable blood test for monitoring inflammatory response and it also helped in prediction of outcome of stroke patients in the shorter duration. Erythrocyte sedimentation rate > 28 millimeter/hour reflects a worse prognosis.

An association was established between Erythrocyte sedimentation rate, Fibrinogen and cerebro-vascular flow. It showed that higher Erythrocyte

sedimentation rate during acute stroke can indirectly indicate a markedly higher rise in fibrinogen levels and a marked decrease in blood flow to cerebrum, resulting in worsening of lesions.

The relationship between Erythrocyte sedimentation rate and the outcome in stroke patients can also represent the alterations in the usual level of natural occurring anti-coagulants.

In recent times a strong association was identified between Erythrocyte sedimentation rate & C4b-BP protein, a HMW protein which has a site for attachment of Vitamin K dependent protein S, a coagulation inhibitor.
Whenever protein S binds to C4b-BP, the former will lose its anti-coagulant property. Hence alterations in C4b-BP protein can result in thrombosis.

Early raise of Erythrocyte sedimentation rate is an excellent marker of poorer outcome in initial period in patients with stroke.

As the details obtained from this test is seen with the severe nature of cerebrovascular accidents at hospital entry, the nature of clinical onset, a sensitive & specific prediction of functional outcome can be obtained for the shorter-term.

Hence measuring Erythrocyte sedimentation rate at the time of admission for patients with symptoms of stroke gives physicians with an easy cheaper and beneficial test when early imaging usually inappropriately estimates the actual

extent of cerebral infarcts and reduces the specificity of those models depicting functional outcome after acute Ischemic stroke.

URIC ACID:

It is an aqueous antioxidant present abundantly in Homo sapiens, forming up to 2/3rd of plasma free radical scavengers & is efficient in neutralising OH^-, $H_2O_2^-$ radical's thereby preventing per-oxidation of lipids. In a number of organs Uric acid levels raises in ischemic events with oxidative stress. Higher levels act as a mechanism which protects from free radical scavenging.

Synthesis:

It is the ultimate product when purines are metabolised in humans.

When compared to allantoin a soluble product produced in lower animals, UA is weakly soluble product of metabolism of purines in human beings. UA levels are higher because of the lack of hepatic enzyme - uricase as well as due to reduced elimination of uric acid in urine.

Source:

→ 2/3rd Endogenous production

→1/3rd Dietary source.

Metabolism:

Seventy percent excretion is through renal mechanism and 30 % by GIT.

Uric acid levels in blood depend on a proper balance between:

→Purine metabolism &

→Urate rate of elimination

Any one mechanism when affected can cause increasing levels though decreased elimination is responsible for increasing levels in most of the patients.

A Uric acid- Anion exchanger URAT1 is seen in the brush border of the renal tissue. Another human organic anion transporter is seen to be blocked by drugs with uricosuric actions, while another uric acid transporter facilitates uric acid to be pushed out of the cell. All these transporter mechanisms are responsible for the secretion and re-adsorption in renal tissues.

Uric acid secretion has a strong correspondence with the its serum concentration, as a slight raise in the serum levels causes a drastic increase in uric acid elimination. Reduced secretion in tubules occurs in patients having acidosis as the organic acids that assimilate compete with uric acid for secretion. At last, increased re-adsorption of urate distal to the site of its secretion is the main mechanism causing higher levels of urate in those on diuresis and those having diabetes insipidus.

Over production :

→ exogenous (purine rich diet)

→ endogenous (increased catablolism).

→Sometimes there is a deficient HGPRTase eg: Lesch Nyhan syndrome,.

→Blast Crisis of acute leukemias

→Cellular death due to rhabdomyolysis

→Glycogenoses types 3,4 & 7 causes hyperuricemia from breakdown of Adenosine-Tri-phosphate in muscle.

→Ethanol consumption (rapid catabolism of ATP in liver & production of substances that competes with uric acid to be secreted in tubules.

Prevalance of Hyperuricemia:

- ➔ Higher in elderly people > 65 years
- ➔ Sex wise distribution
    - When age <65 M: F prevalence – four times more in males
    - When age <65 M: F prevalence – three times more in male

Courtesy: Study from Japan.

Disability and Death

More in patients with

→Hypertension

→Females & aged people. (etiology not known)

Hyperuricemia is an important marker for comorbidity risk factor than a causative factor.

The normal urate levels in children is lesser. (Reference range is 5mg/dl).

Males →7 mg/dl

Females→ is 6 mg/dl.

Sources:

→Poultry & animal products mainly organs.

→sweetbreads

→anchovies

→sardines

→ liver, beef brain & kidney

It can be raised secondary to increasing fructose intake & decreased renal elimination with high purine in diet.

RELEVANCE TO STROKE:

In experimental models with animals, local Uric acid raises in significant levels in cerebral injury.

As in one case: In Rat, MCA artery obstruction results in raise in cerebral UA concentrations to significant levels that persists for many days Post injury. These observations has prompted an interest in the potential impact of
Uric acid levels in the setting of an acute event of ischemic stroke. Uric acids role as an independent risk predictor in vascular disease was questioned for several years. Various studies do indicate that elevated concentration of uric acid can be important in prediction of risk of stroke. Further treatment to decrease uric acid has shown to decrease the cardiovascular disease mortality.

Those with Non insulin dependent Diabetes have a 2 fold to 4 fold risk of showing effects of atherosclerotic disease like stroke. It is indicated that Increased uric acid levels is an important factor in the prediction of stroke in middle aged individuals with Non insulin dependent Diabetes independent of rest of the CV risk factors.

This Uric acid concentration is a useful, simple marker to select and treat patients at risk. SUA has been recently associated with insulin resistance.

Urate is a marker of oxidative stress. It has an important role as an antioxidant. It can also play the role of a peroxidant, when at greater levels. Whether rising urate levels in conditions related to oxidative stress like atherosclerotic stroke is a preventive response or the main cause is unclear. Through researches it is identified that hyper-uricemia mediated oxidative stress act as an important mechanism in Metabolic Syndrome.

Various studies does indicate that Urate levels were markedly increased in those who succumbed to stroke when compared to the ones who got discharged thereby proving that it is useful as a marker for increased risk of stroke & risk stratification post stroke. Serum Uric Acid is as an Independent Predictor of early mortality post stroke as well as for higher vascular event rates. Though urates role in far from being certain, therapies to lower uric acid levels is definitely worthy.

FIBRINOGEN

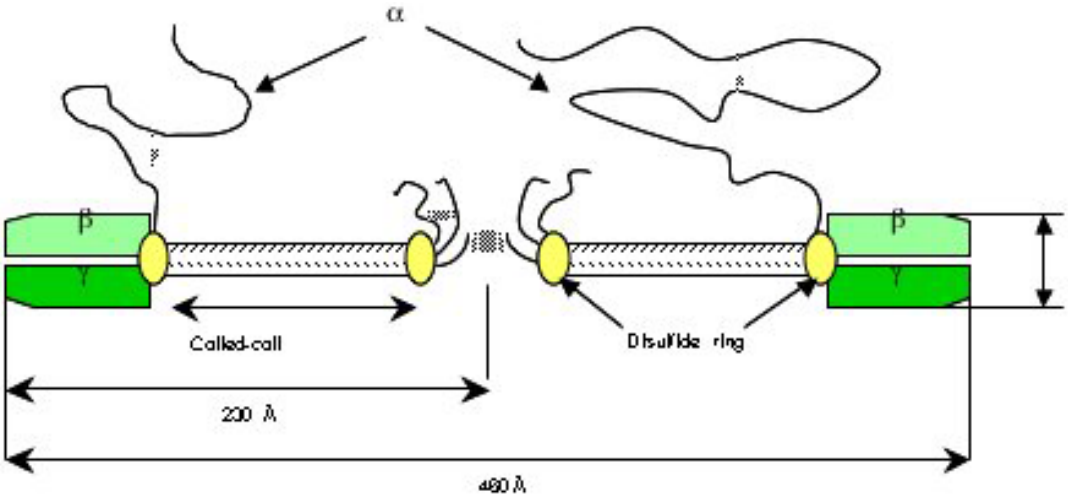
Fibrinogen – A Glycoprotein that consists of 3 pairs of non-identical polypeptide chains namely Aα (alpha), Bβ(beta) and γ(gamma) chains 4.

In the first phase of thrombus formation soluble fibrinogen is converted into insoluble fibrin by thrombin. Thrombin cleaves Aα and Bβ chains thereby releasing fibrinopeptides, these fibrinopeptides initiate a process in which fibrin monomers begin to gel. These fibrin monomers polymerise to form fibrin polymers. This process continues and elongation of polymers causes formation of protofibrils. Once a critical mass of long protofibrils is established, the protofibrils form lateral contacts with other protofibrils thereby forming fibrin clot. Fibrin clot thereby potentiates formation of thrombosis.

Various studies show us that higher levels of fibrinogen levels have a strong correlation with the athero-sclerotic complications namely MI & Cerebrovascular events. Thrombosis is found to play a significant role in both & Fibrinogen has an important role to play in thrombosis.3 Hence identifying the association between thrombosis and fibrinogen can increase the predictive value of this glycoprotein and suggest a different line of treatment in stroke patients.3 Hence the study design is such as to find out the relationship among plasma fibrinogen and acute stroke. Higher levels of Fibrinogen are an independent risk factor in aetiology of Stroke. It assists in predicting adverse events in future. Hence, Estimation of levels of Fibrinogen and treatment is valuable to improve the outcome of the patient.

STRUCTURE :

DIAGRAM TO ILLUSTRATE FIBRINOGEN STRUCTURE



Liver synthesize fibrinogen and secrete it in to plasma. The molecular structure as revealed by Electron microscopy is a large trinodular di sulphide bonded glycoprotein with 2 evenly symmetric molecules. Each half has 3 distinct polypeptide chains namely Aα, Bβ and γ chains. The molecular mass of whole molecule is 340000 dalton, length is 45 nm, diameter is 9 nm. Its central nodule i.e E –domain is 5 nm in diameter. It has the NH – 2 terminal of all six polypeptide chains and thus it forms the NH – 2 terminal disulphide knot.

The outer D-domain nodules are made of the C-Terminal two thirds of both the Bβ and γ chains. Xray diffraction studies indicates that the Bβ, γ chain each form an independent subdomain within the D- domain. These two subdomains are located diagonally along the long axis of the molecule. Between the E and D domains, a stretch of approximately 120 amino acids is present from each of the 3 chains which form a α-helical structure - the “coiled coil

domain". This part of the molecule is assisted on either side by a set of disulphide bonds which is the disulphide ring. This plays a major role in making fibrin strong & proteolysis resistant.

The Aα chain is a 610 aminoacid polypeptide. It's divided in to three seperate domains. The first section (Aα chain - residues 1-194) has a region (residues 45-161) linked to the Bβ and γ chains by disulphide bonds. This section forms part of the α-helix or coiled coil domain. This part also has fibinopeptide –A (residues1-16) and the polymerization site in the E-domain.

The middle third of the molecule (residues 240-424) is rich in apolar aminoacids and has ten tandem repeats each 13 aminoacids long. The region bridging these two sections (195-239 residues) is made up of domain which has high amounts of pralines and several plasmin cleavage sites.Two glutamine residues in the middle serves as an important receptor site for factorXIII a cross linking.

The hydrophilic C terminal third of the molecules (residues 425-610) act as cross-linking sites for fibronectin and α-2 antiplasmin. Residues 95-97 &572-574 present in Aα chain act an important role in cellular adhesions.

The Bβ polypeptide chain has 461 aminoacids and has 3 sections. Initial 80 residues is made of fibrinopeptide B sequences (1-15) as well as a site which supports endothelial cell spreading and proliferation (15-42). Residues 81-192 linked to Aα and γ chains through disulphide rings .It forms the coiled

coil domain. The C-terminus of the Bβ chains forms subdomain of the D-domain which is independently folded.

The γ chain is 411 aminoacids long. It is divided in to 3 sections. Unlike the other chains, it has no fibrinopeptide at its NH2 terminal. The first 18 aminoacids of the γ chain form the disulphide knot portion of the NH2 terminal. Middle segment consists of aminoacids 19-135. It also has the disulphide rings that connect this region to Aα and Bβ chains in the coiled coil domain. The C-terminal portion which has aminoacids 136-411 forms a globular sub domain of the D domain. In this part is the D-domain polymerization site as well as the Factor XIIIa cross linking sites and the binding domain for aggregation of platelets (400-411 residues).

The γ chains have two forms γ and $\gamma^{1.}$ The latter contains an extended C terminal. It is produced by polyadenylation of the last intron of the γ gene chain. Studies have shown γ^{1} is a carrier for zymogen of factor XIII in circulating blood.

SYNTHESIS: Plasma fibrinogen is synthesized exclusively by the hepatocyte, and the synthesis of the three chains is controlled by 3 different genes localized on 4th Chromosome (ch4q23-q32). $T_{1/2}$ is of 72-108 hours. The turnover rate of fibrinogen is about 1.7-5 gm/day (30-60mg/kg/day).

Normal Fibrinogen levels – 233 to 496 mg/dl

FUNCTION:

Fibrinogen plays the central role in three major functional processes.

1. The soluble fibrinogen molecule is converted into insoluble fibrin during the process of blood coagulation.

2. The polymerized fibrin serves helps in assembling & activating the fibrinolytic process, which modulates fibrin deposition and clot dissolution.

3. Fibrinogen binds to vascular cells such as platelets, where it supports platelet aggregation by binding to platelet GP IIa-IIIb receptors and to endothelial cells, where it participates in tissue repair.

The transformation of fibrinogen → insoluble fibrin has 3 distinct phases.

1. Thrombin cleaving the fibrinopeptide

2. Fibrin polymerization.

3. Fibrin stabilization, via cross linkage by XIII a factor

First up, the Arginine16- Glycine 17 bond of the Aα, the Arginine 14- glycine 15 bond of Bβ chain is cleaved by thrombin, resulting in the release of two molecules of fibrinopeptide A(FPA) and two of fibrinopeptide B(FPB) per molecule of fibrinogen. Fibrinopeptide release from the constituent Aα and Bβ chains forms a fibrin (monomer), and its constituent chains of which are now referred to as the α-, β- and γ- chains. The proteolytic cleavage of the FPA occurs prior to and more rapidly than that of FPB which is sufficient to induce clot formation. The polymerization process involves the reciprocal non covalent

interaction of molecular determinants in the fragment E region of the molecule, which are exposed by the removal of FPA, with complimentary binding sites located in the fragment D region of an adjacent fibrin monomer. The resulting dimer which is arranged in a half- staggered overlap, continues to grow in length by the staggered addition of fibrin monomers, resulting in the formation of a two-stranded, half-staggered polymer referred to as a protofibril, the basic structural unit of the fibrin clot. The half-staggered polymerization process brings two D domains of longitudinally aligned fibrin molecules of each row of the protofibril into close contact with one another, resulting in further stabilization of the non covalently associated fibrin protofibril. Polymerization continues with the formation of long, double-stranded protofibrils that ultimately associate laterally to form thick fibrin 9 bundles. The cleavage of FPB occurs mainly during the initial phase of fibrin polymerization and exposes determinants that are complementary with binding sites present in the C Terminal portion of the Alpha-chain. This interaction seems to increase the rate of formation of thin fibrils, as well as the lateral aggregation to form thick fibrin fibers. The three-dimensional fibrin matrix is completed by branching of the fibers at specific contact points located in the fiber bundles. Several of the polymerization sites within fibrin have been identified. The N-terminus of the fibrin α-chain participates in the interaction of the A determinant with the complementary binding site located in fragment D, where a segment of the γ-chain is known to participate in fibrin polymerization. In addition, the N-

terminus of the fibrin β-chain participates in the assembly of fibrin by binding to a complementary site present in the C Terminus of the A-alpha Chain.

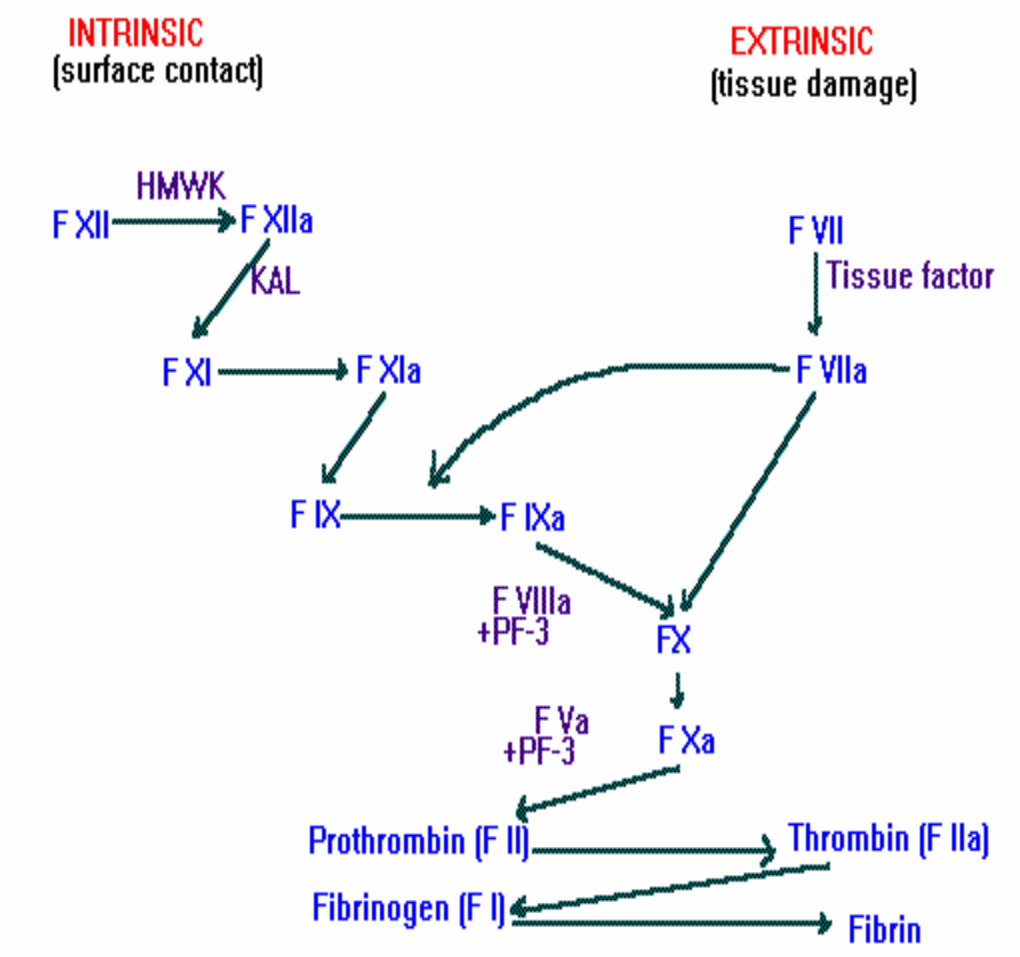
The final stage of fibrin formation is characterized by the factor XIIIa-mediated formation of covalent amide bonds between the ε-amino groups of specific lysine residues and γ- CONH2 groups of certain glutamine residues. These covalent bonds are first formed at the DD contact between the γ- chains of two molecules. The dimerization of the γ-chain formed by bridges between Lysine of one γ-chain and glutamine of another is then followed by progressive covalent cross-linking of multiple α-chains. Cross-linking at branch points also produces D-trimers or D-tetramers. As a result of this covalent stabilization, the clot is rendered more compact and resistant to both mechanical disruption and dissolution by plasmin. In addition to plasma fibrinogen, the circulation blood contains a very small pool of fibrinogen, which is present within the platelet α-granules. Some studies have shown that fibrinogen is synthesized by megakaryocyte, but more recent investigations have 10 demonstrated that platelets & megakaryocytes have the ability to internalize fibrinogen from plasma by a process mediated by glycoprotein IIb/IIIa. Plasma fibrinogen exhibits γ-chain heterogeneity due to differential splicing of the hepatic m-RNA. This heterogeneity is manifested by the presence of a minor component, termed γ1, in which the last four amino acids of the γ-chain are replaced by an extended COOH terminal sequence.

The γ1-chain is not present in platelet fibrinogen and does not support platelet aggregation, probably due to the lack of interaction of γ1 with glycoprotein IIb/IIIa of the platelet. Studies of families with various genetic dysfibrinogenemias have provided conflicting results concerning the presence of the mutant fibrinogen within the platelet. While fibrinogen Paris-I was not found in platelets, fibrinogen Oslo-I was.

However, the discrepancy between the molecular and functional properties of plasma and platelet fibrinogen in these variants could depend on the ability of the platelet and megakaryocyte to internalize the abnormal fibrinogen. Platelet fibrinogen is secreted after stimulation and plays a role in supporting haemostasis.

Fibrinogen concentration ranges from 150-400mg% which far exceeds the minimum concentration of 50-100mg% necessary for haemostasis.

DIAGRAM ILLUSTRATING ROLE OF FIBRINOGEN IN COAGULATION CASCADE



FIBRINOGEN ASSAY.

CLOTTING RATE ASSAY/CLAUSS ASSAYS

The main technique was given by Von Clauss, based on the rate of clot formation in dilute citrated plasma following the addition of thrombin. The clotting of dilute plasma is inversely proportional to the plasma fibrinogen concentration when high concentration of thrombin is used. The quantity of

thrombin used must ensure that the clotting time is always dependant on the level of fibrinogen in plasma sample. We add thrombin (conc between 35-200μ/ml) usually 100μ/ml for dilution of test plasma & clotting time calculated. Clotting end point is measured by either mechanical or photo-optical means, as these methods have shown excellent cross correlation and precision, results are compared with a calibration curve. The net result obtained is expressed in mg/dl. Drawbacks are that it is comparatively time consuming & needs a higher grade of expertise when manually done, as the endpoint is pretty difficult to find with an increasing dilutions of std. plasma. As this type of assay measures the time to formation of a detectable clot, the presence of inhibitors of fibrin polymerization, such as fibrinogen and 14 fibrinogen degradation products results in under estimation of the actual fibrinogen concentration.

At present commercial reagents as well as automated methods are being used by most labs and there are essential difference based on the type of analyzer used. Yet they are less likely to create a significant impact clinically. The precision is within reasonable limits when normal plasma is used and assessment is carried out by optical methods (typically3-7%) whereas by mechanical means it comes to 6-9%.

Ideal recommended anticoagulant for this assay is Tri Sodium Citrate at a concentration of 0.105-0.109m (9 parts blood with 1 part of anticoagulant). Blood collection must be aseptic and as fast as possible avoiding significant stasis. Before Estimation of fibrinogen collected samples are checked for the presence of clots by inversion technique .Sample with such evidences or those with hemolysis must be rejected. Platelets are removed (<1lakh/Litre), by centrifugation. Hyperlipidemia or Hyperbilirubinemia can result in problems with analysis when optical methods of are used. Storage should be in room temperature for minimum of four hours before processing. Thawing leads to cryo-precipitate formation which has fibrinogen. This can affect the values.

3.1.5 REGIONAL VARIATIONS IN PLASMA FIBRINOGEN LEVELS

Several epidemiological studies have shown that normal plasma fibrinogen levels range from 2.3-4.0 gm/dl. The method of measurement has strong influence. Ernst has shown that those studies which employed the standard method on thrombin coagulation time (clauss assay), the mean fibrinogen levels varied from 2.3-4.1 gm/dl. This could not be attributed to age and sex because only men were selected for this analysis and patient's ages were similar. The regional variations in the fibrinogen levels are due to undefined environment factors and are unrelated to patient characteristics.

FIBRINOGEN ABNORMALITIES:

Classified as congenital or acquired, with both groups manifesting quantitative defects or qualitative differences of fibrinogen molecules. In few instances, both quantitative and qualitative abnormalities can be present in the same patient.

a) CONGENITAL DISORDERS

i. Congenital afibrinogenemia and hypofibrinogenemia

They are familial and cause bleeding disorders of varying severity from birth. Sometimes low fibrinogen may be an abnormal molecule then it is called hypo-dysfibrinogenemia. CT, PT and aPTT are abnormal.

ii. Congenital dysfibrinogenemia.

Due to synthesis of a structurally varied fibrinogen molecule which expresses altered properties and also exhibits an abnormal thrombin mediated conversion to fibrin.

Such alterations are due to changes in few phases of fibrinogen catabolism.

These include:

→ Fibrinopeptides release is reduced.

→ Fibrin polymerization is affected

→ Failure of polymerized fibrin to undergo normal covalent stabilization by factor XIIIa.

→ Abnormal interaction with platelets, endothelial cells or calcium.20

Most patients are asymptomatic. Prothrombin time is prolonged. Plasma fibrinogen concentration is normal when measured immunologically and the discrepancy between clotable protein and immunologically measured fibrinogen is a characteristic feature of dysfibrinogenemia.

b.) ACQUIRED DISORDERS

HYPERFIBRINOGENEMIA

Various causes for elevated fibrinogen level are,

1. **Race:** Fibrinogen is about 0.2gm/L higher in blacks than in whites

2. **Males:** Males have a higher fibrinogen levels than females

3. **Smoking:** There is a positive correlation between smoking and plasma fibrinogen levels; Fibrinogen level begins to fall soon after smoking is discontinued. The consistent observation of higher plasma fibrinogen levels in heavy smokers, independent of age, may be explained by two hypotheses;

a) Smoking may lead to endothelial damage resulting in activation of the coagulation system.

b) Smoking activates lung macrophages which release interleukin-6 increasing liver synthesis of fibrinogen.

5. Physical inactivity: There is an inverse relationship between physical activity and fibrinogen concentration.

6. **Diet:** Diet rich in carbohydrates and fat and diet poor in ω-3 and ω-6 PUFA's and fibre are associated with raised fibrinogen levels.

7. **Excess body weight:** In obese patients, both viscosity & fibrinogen levels are

Increased.

8. **Hyperlipidemia:** There is a strong positive correlation between the fibrinogen & cholesterol levels, high LDL, high Lp(a) and elevated triglycerides. It is also consistent with an increased risk of atherosclerosis, thrombotic events in dyslipidemic patients.

9. **Diabetes Mellitus:** A strong association is present between HbA1c & plasma fibrinogen levels. In Scottish Heart Health Study, this was proved.

10. **Hypertension:** Greater levels seen in hypertensives compared to normotensives. Despite patient being mildly hypertensive, fibrinogen levels are higher than normotensive controls.

11. **Ischemic heart disease:** There exists a consistent relationship with the extent, and severity of heart disease.

12. **Left ventricular dysfunction:** There is an increased risk of intracardiac thrombus and systemic thromboembolism in patients with poor cardiac function, especially in those with ventricular aneurysm and dilated cardiomyopathy. Thrombosis risk in patients with left ventricular dysfunction is increased because of increased fibrinogen levels as compared to patients with normal left ventricular function.

14. **Psychological and mental stress-** It has been shown to increase plasma fibrinogen concentration.

15. **Cerebrovascular disease-** Increased fibrinogen was correlated with stroke and TIA incidence and progression of carotid atherosclerotic lesion. Peripheral

vascular disease is associated with increased fibrinogen concentration. Fibrinogen levels have been found to be higher in those persons who are taking oral contraceptives and in postmenopausal age.

18. **Genetic factors-** There is a significant role for it to play as genetic inheritability can be responsible for up to 51% of variance of the plasma fibrinogen level. Variation at the beta fibrinogen locus has been thought to affect fibrinogen concentration, because the beta gene control formation of Bβ chains, the rate limiting step in fibrinogen synthesis. Individuals with B1B2 genotype who have high fibrinogen levels are at increased risk of atherosclerosis.

HYPOFIBRINOGENEMIA -occurs due to

i. Decreased hepatocyte biosyntheses due to fulminant hepatic failure, decompensated liver cirrhosis.

ii. Disseminated intravascular coagulation due to increased consumption.

iii. Use of drugs like L-asparaginase, valproic aced.

iv. Alcohol consumption has an important effect on reducing the fibrinogen levels. A decrease of approximately 0.78% per 10gm of alcohol consumed has been noted.

v. Fibrinolytic therapy reduced fibrinogen levels for a day or two.

DYSFIBRINOGENEMIA:

Dysfibrinogenemia of liver disease: About 50% of patients with cirrhosis, hepatitis or hepatoma exhibit dysfibrinogenemia which is characterized functionally by impaired polymerization of fibrin.

Similar changes have also been observed in hypernephroma as a part of paraneoplastic syndrome.

Antibodies against fibrinogen can cause functional abnormalities of fibrinogen as seen in SLE, ulcerative colitis and post-necrotic cirrhosis or sometimes can be idiopathic. Inhibition of fibrin monomer polymerization is seen in multiple myeloma.

STUDY IMPORTANCE:

Fibrinogen levels have increased in patients with stroke. Higher levels are seen in ischemic stroke compared to hemorrhagic stroke. Increasing evidence suggests that fibrinogen is important in the development of premature atherosclerosis. Levels > 350 mg/dl is a risk factor for coronary artery disease and stroke. There is higher risk of future CV events in those who survive from stroke.

Fibrinogen molecules bridge adjacent platelets together to form platelet aggregates and arterial thrombosis leading to ischemic stroke. It is a risk factor for further recurrences of stroke apart from age, smoking, hypertension, diabetes and other risk factors. Compared to altered lipid profile in the form of

high LDL levels, triglycerides and low HDL levels, fibrinogen is a better predictor of future recurrences of stroke and adverse cardiovascular events. Hence, fibrinogen levels are to be measured in patients with stroke at the earliest and to be treated.

Fibrinogen also interacts with monocytes/macrophages and these play a significant role in atherogenesis, and the binding of these two is responsible trigger for pro-coagulant activities.

Study by Shao-Yuan Chuang et al showed that in addition to hypertension and diabetes, fibrinogen independently predicted future ischemic stroke risk and altered lipid profile did not independently predict cerebral infarction.

Study by Ligeesh A et al showed higher plasma fibrinogen levels in ischemic and hemorrhagic stroke, comparatively higher levels in ischemic stroke.

Study by Kofoed S C et al showed elevated fibrinogen predicts future ischemic strokes particularly in men.

Study by Mario Di Napoli et al showed that higher levels have a greater risk if cardiovascular events in post stroke patients.

Study by Ziakas G N et al showed significant relation between high cholesterol level, high fibrinogen level and ischemic stroke.

BARTHEL INDEX:

The functional Outcome is measured using the Barthel index score. The index is used to record what a stroke patient does. First came in to limelight in 1965 with a score of Zero to Twenty. Despite the fact that the initial version was still in use, Granger et al modified the score during early seventies, when he included zero to ten points for each variable. Again changes were done in 1989.

This index had shown a worthy inter-rator reliability (0.95) & a high correlation i.e 0.74 up to 0.8, compared with other physical disability measurements. The reason for designing the modified Barthel index was that the first scale brought out was not sensitive to any change and it also had only arbitrary scores.

Otherwise known as the **Barthel ADL index** it is an ordinal scale helping us to measure performances in ADL - activities in daily living. Every performance item is given a rating using this scale with a score for every level exhibited by the patient. There are 10 different factors depicting ADL & mobility. Larger number will have an association with a higher probability of the patient being able to live independently at home after getting discharged from hospital

There are 10 items indicating a person's daily functions.

FEEDING	BLADDER
BATHING	TOILET USE
GROOMING	TRANSFERS (bed/chair)
DRESSING	MOBILITY (levels)
BOWELS	STAIR

USAGE : helps in determining a basal functional level of the patient and useful in monitoring any improvement in ADLs over time. Scoring is done on the basis of whether they receive help for doing the task.varies between 0, 5,10,15 Summation of scores of each of the items is done to get a final score. Greater the total score means more "independent" the patient is. A patient is independent when he does not need any assistance for any portion of the task. When he/she is able to do 50% of task independently “middle" score is given. In this manner a total score is calculated.

Functional status was measured with Barthel Index of ADL. Accordingly, they were divided into 3 groups.

Score	Disability
< 41	Severely
41-60	Moderately
>60	Mildly

AIMS AND OBJECTIVES:

1. TO STUDY THE BIOCHEMICAL PARAMETERS URIC ACID CRP ESR FIBRINOGEN IN ISCHEMIC STROKE PATIENTS AT GOVERNMENT STANLEY HOSPITAL

2. TO ASSESS FUNCTIONAL OUTCOME IN THESE PATIENTS USING BARTHEL INDEX AT ADMISSION AND AT DISCHARGE

MATERIALS AND METHODS

PLACE OF STUDY:

DEPARTMENT OF GENERAL MEDICINE, MEDICAL OPD, MEDICAL WARDS AND IMCU AT STANLEY MEDICAL COLLEGE AND HOSPITAL, CHENNAI.

SAMPLE SIZE :

75

DURATION:

JAN 2014 TO SEP 2014.

STUDY DESIGN:

PROSPECTIVE OBSERVATIONAL STUDY

ETHICAL COMMITTEE APPROVAL:

THE ETHICAL COMMITTEE APPROVAL WAS OBTAINED FOR THIS STUDY

INCLUSION CRITERIA

1. Any Patient coming with symptoms suggestive of Acute Stroke to medical outpatient department, wards and Intensive care unit.
2. Proven by Imaging as Ischemic Stroke.
3. Patients age more than 18 years

EXCLUSION CRITERIA:

1. Hemorrhagic stroke patients
2. Patients with any source of Sepsis / Infectious Disease in prior 4 weeks.
3. Patients presenting after 72 hours of onset
4. Patients having evidence of renal disease, active hepatic disease, history of prior MI/Ischemic Heart disease or surgery within preceding 3 months.
5. Patient with any form of Arthritis
6. Recent Trauma/ burns.
7. Patients with prior history of stroke or TIA's.
8. Patients on any lipid lowering agents including fibrates.
9. Patients with venous stroke and Stroke due to Tumours.

CONSENT

The study group thus identified by the above criteria (inclusion and exclusion criteria) was first instructed about the nature of the study. Willing participants were taken up for this study after getting a written / informed consent from these patients or their relatives in the local vernacular language.

STUDY SUBJECTS:

All the patients who fulfilled the inclusion criteria above 18 years of age and both genders were included in this study. The included patients were subjected to detailed history taking, complete physical examination and the relevant laboratory investigations as per a proforma, exclusively designed for the study.

RESULTS & DISCUSSION

The study includes total number of 75 patients. Data were collected and final analysis was made.

Study Groups

Treatment Groups	Name of Group	Study	Number of Subjects
Group A	Mild	To assess functional outcome in these patients using Barthel index in ischemic stroke patients	75
Group B	Moderate		
Group C	Severe		

Statistics

Descriptive statistics was done for all data and suitable statistical tests of comparison were done. Continuous variables were analysed with the Unpaired t test/Anova and categorical variables were analysed with the Chi-Square Test and Fisher Exact Test. Statistical significance was taken as $P < 0.05$. The data was analysed using EpiInfo software (7.1.0.6 version; Center for disease control, USA) and Microsoft Excel 2010.

Sample Size Calculation

Sample size was determined on the basis of a pilot study in which the prevalence of serum fibrinogen levels was measured at 25%. We calculated a minimum sample size of 72 patients was required in each group, assuming a type 1 error (two-tailed) of 0.05 and a margin of error of 10%. Therefore, the final sample selected was n= 75..

$$n = \frac{t^2 \times p(1-p)}{m^2}$$

Description:

n = required sample size

t = confidence level at 95% (standard value of 1.96)

p = estimated prevalence of malnutrition in the project area

m = margin of error at 10% (standard value of 0.05)

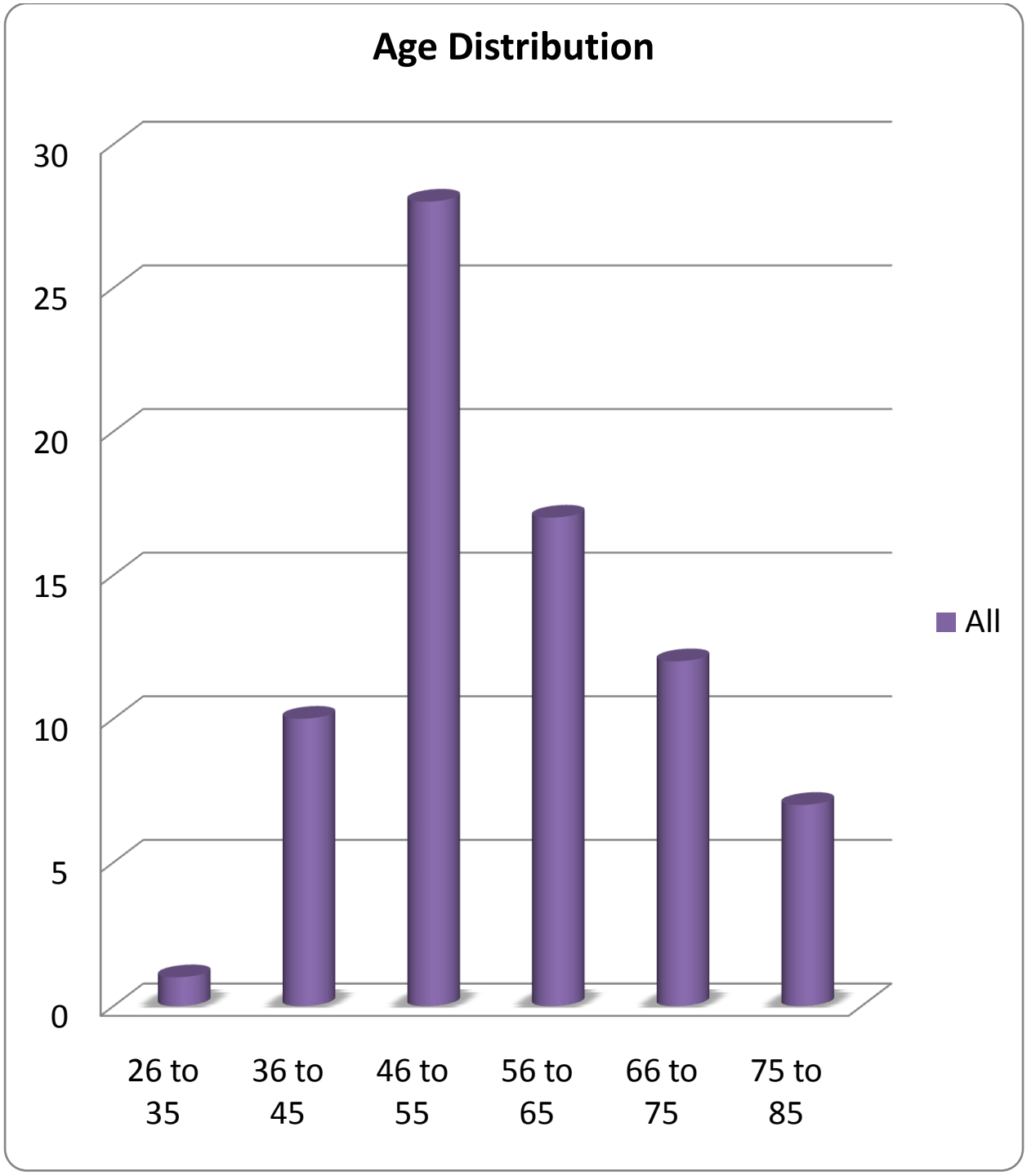
$$n = \frac{(1.96)^2 \times 0.25(1-0.75)}{(0.01)^2}$$

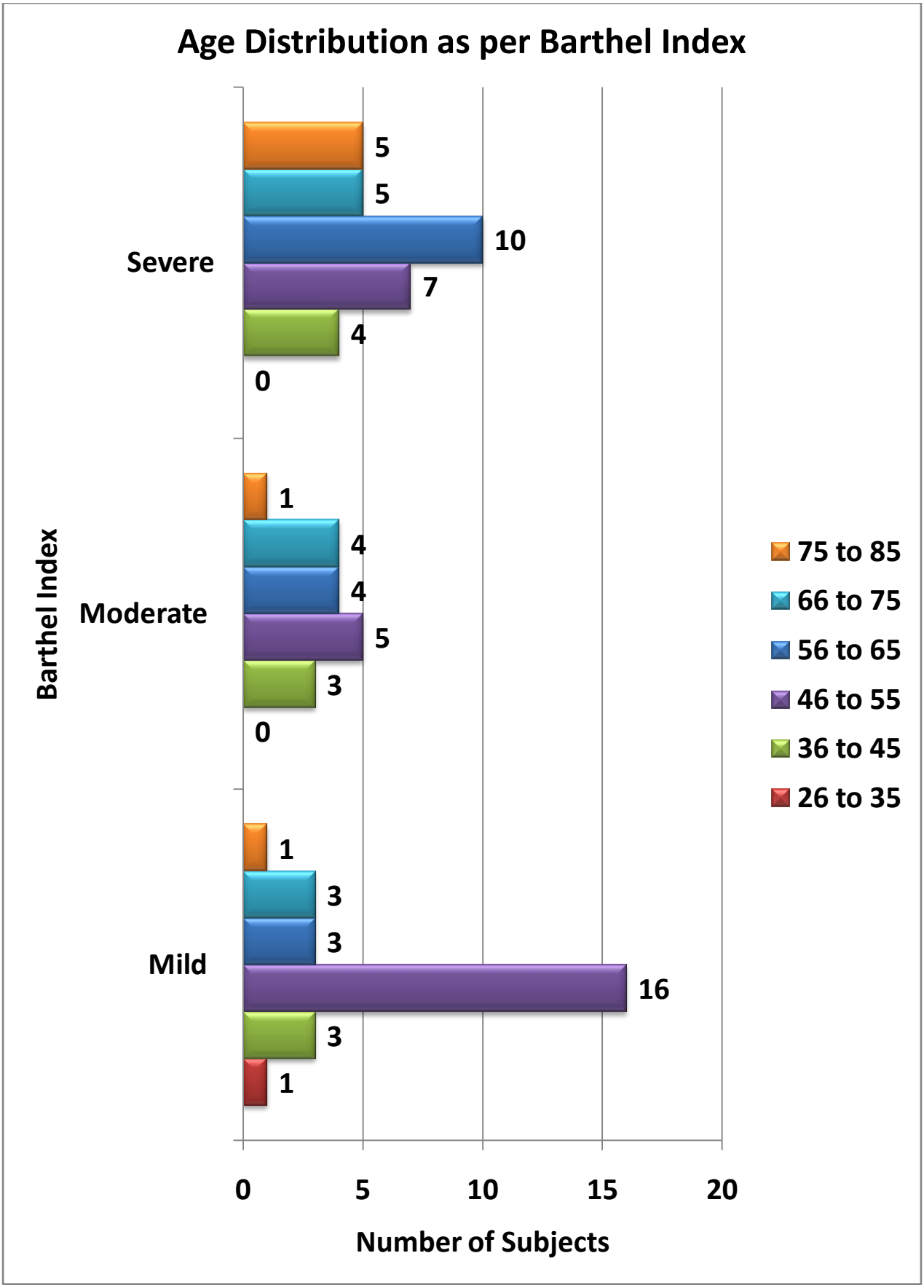
$$n = \frac{3.8146 \times 0.1875}{0.0001}$$

= 138

= 72 per group

Age


Age Distribution
30
25
20
15
10
5
0
26 to 35
36 to 45
46 to 55
56 to 65
66 to 75
75 to 85
All


Age Distribution as per Barthel Index
Barthel Index
Severe
Moderate
Mild
5
5
10
7
4
0
1
4
4
5
3
0
1
3
3
16
3
1
0
5
10
15
20
Number of Subjects
75 to 85
66 to 75
56 to 65
46 to 55
36 to 45
26 to 35

Age Groups	All	%	Mild	%	Moderate	%	Severe	%
26 to 35	1	1.33	1	3.70	0	0.00	0	0.00
36 to 45	10	13.33	3	11.11	3	17.65	4	12.90
46 to 55	28	37.33	16	59.26	5	29.41	7	22.58
56 to 65	17	22.67	3	11.11	4	23.53	10	32.26
66 to 75	12	16.00	3	11.11	4	23.53	5	16.13
75 to 85	7	9.33	1	3.70	1	5.88	5	16.13
Total	75	100	27	100	17	100	31	100

Anova: Single Factor

SUMMARY

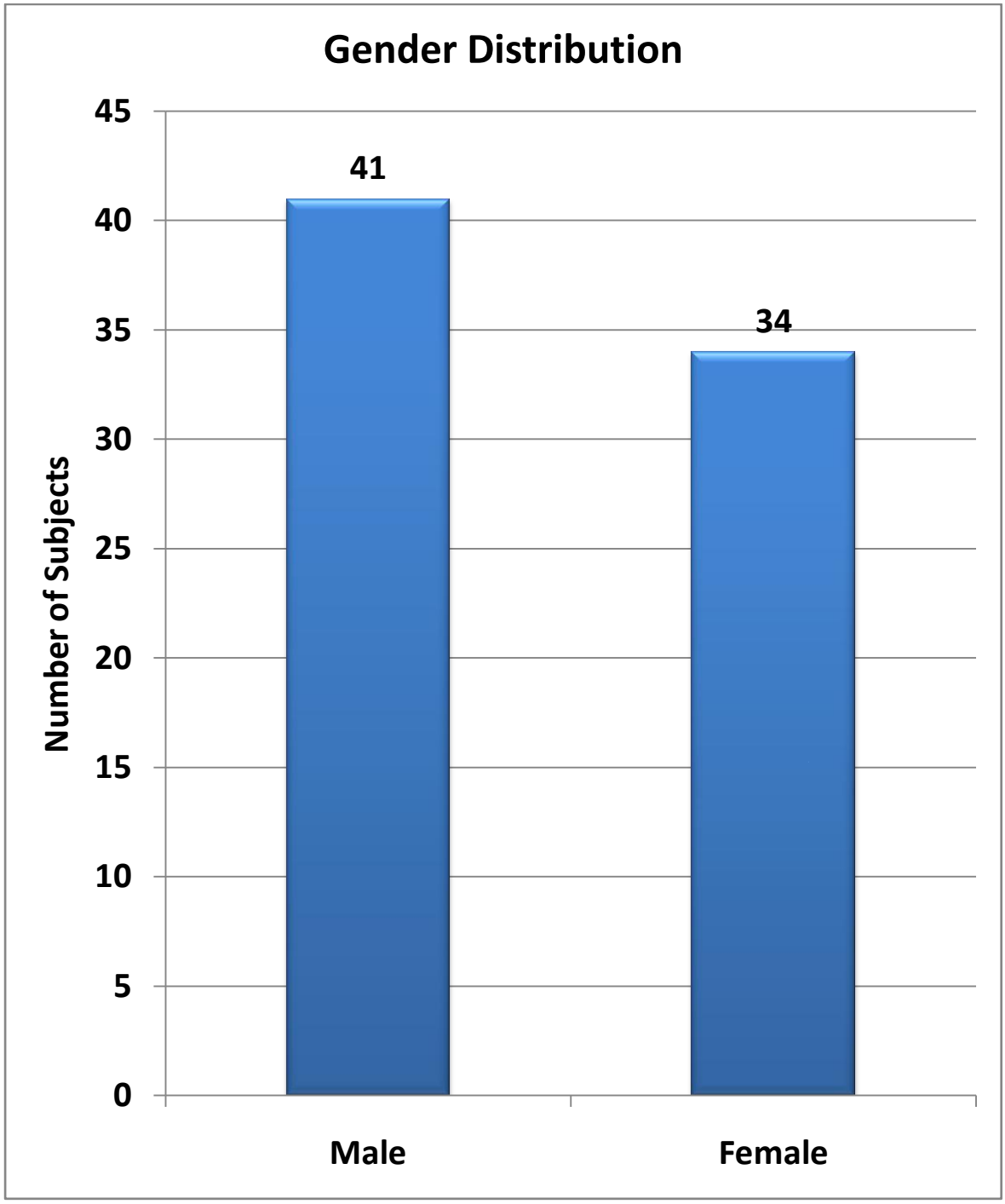
Groups	Count	Sum	Average	Variance
Mild	27	1435	53.14815	100.1311
Moderate	17	982	57.76471	169.9412
Severe	31	1905	61.45161	139.1892

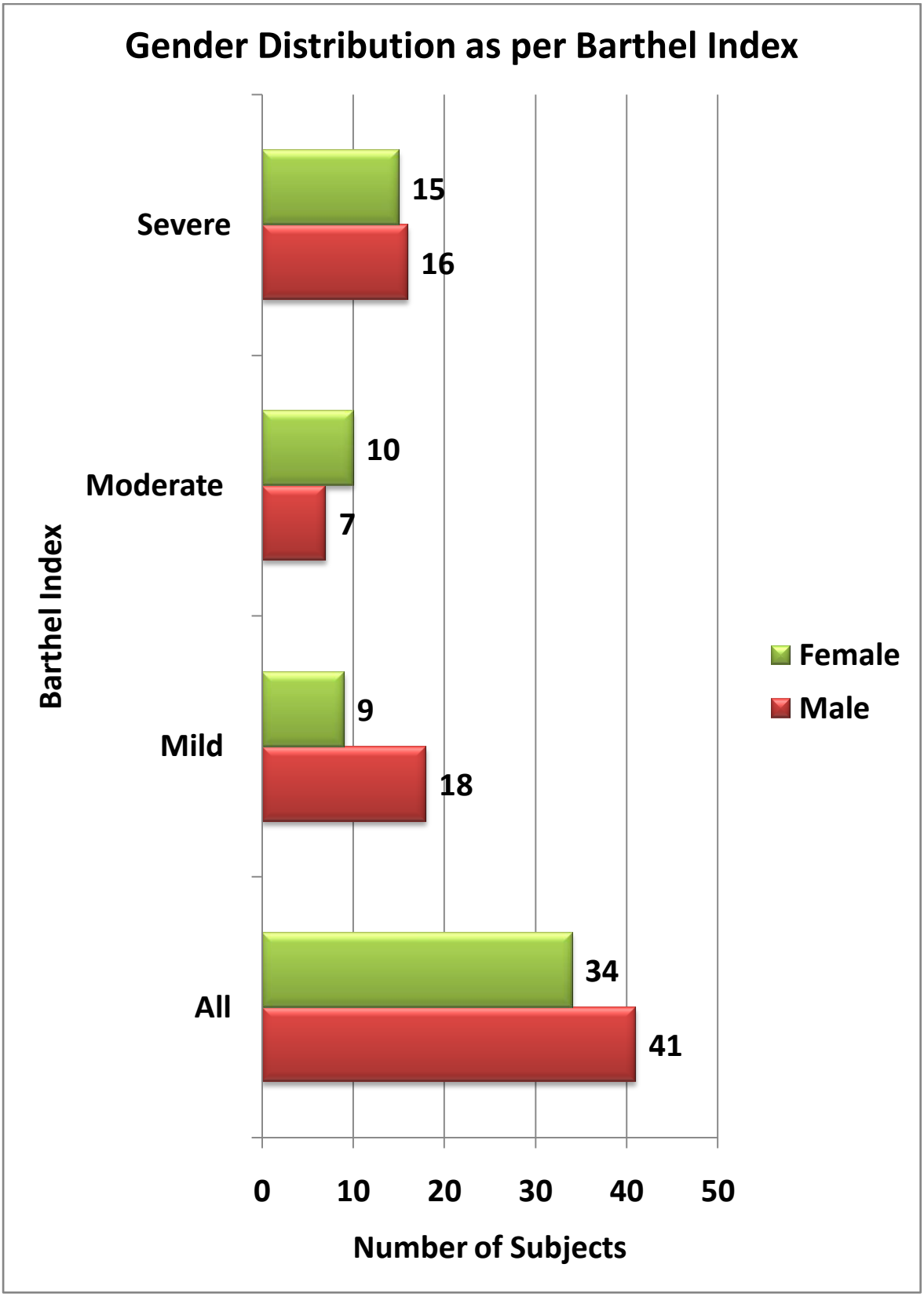
ANOVA

Source of Variation	*SS*	*Df*	*MS*	*F*	*P-value*	*F crit*
Between Groups	995.403	2	497.7015	3.122791	0.27656	3.773907
Within Groups	9498.144	72	131.9187			
Total	10493.55	74				

By conventional criteria the association between the study groups and age is considered to be not statistically significant since p > 0.05.

Gender


Gender Distribution
Number of Subjects
45
40
35
30
25
20
15
10
5
0
41
34
Male
Female

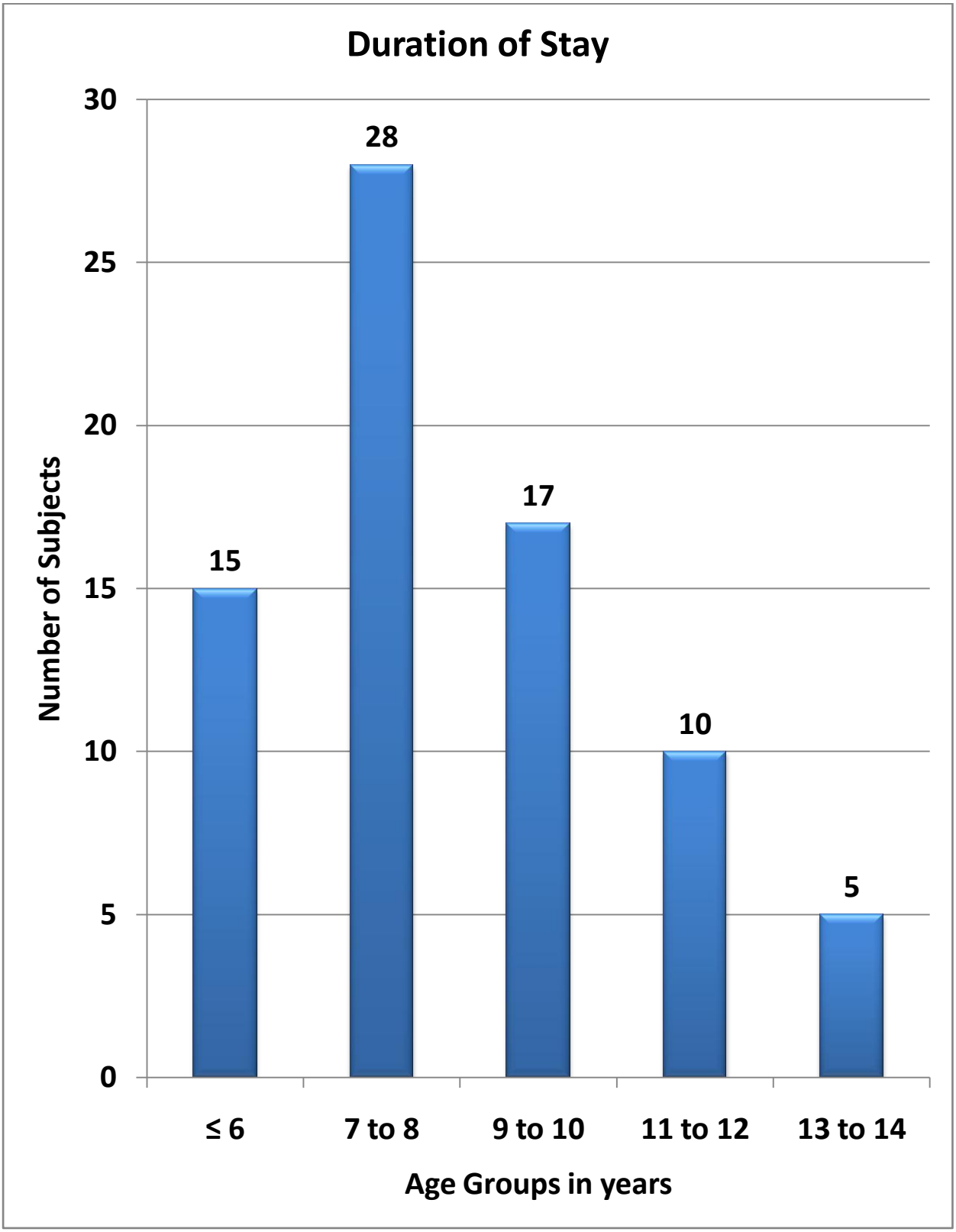

Gender Distribution as per Barthel Index
Severe
15
16
Moderate
10
7
Mild
9
18
All
34
41
Barthel Index
0
10
20
30
40
50
Number of Subjects
Female
Male

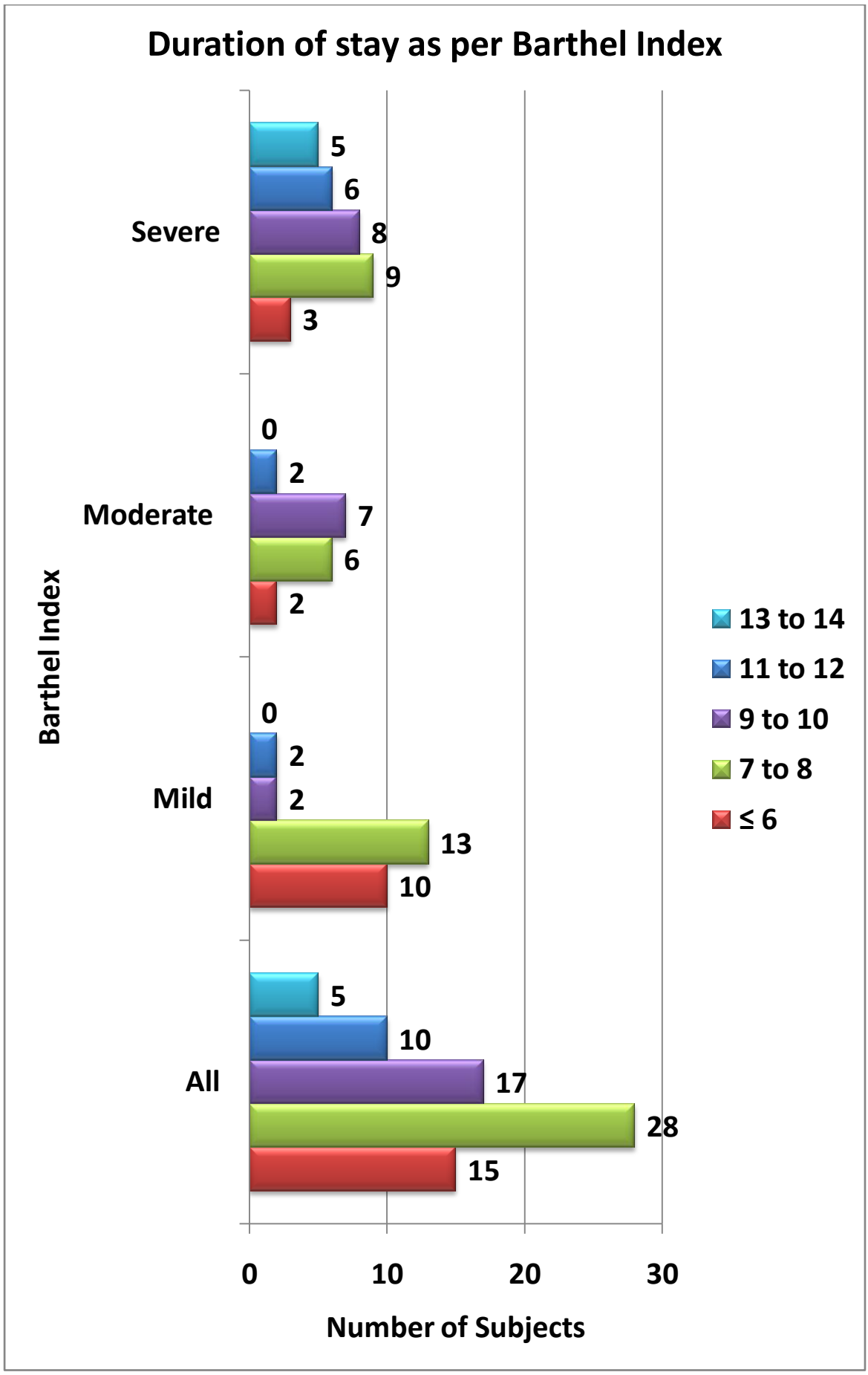
Gender	All	%	Mild	%	Moderate	%	Severe	%
Male	41	54.67	18	66.67	7	41.18	16	51.61
Female	34	45.33	9	33.33	10	58.82	15	48.39
Total	75	100	27	100	17	100	31	100
Chi-square		**2.93**						
Degrees of freedom		**2**						
P value Chi squared test without yates correction		**0.231**						

By conventional criteria the association between the study groups and gender is considered to be not statistically significant since $p > 0.05$.

Since age and gender is not statistically significant, it means that there is no difference between the groups. In other words the groups contain subjects with the same basic demographic characteristics.

Duration of Stay in Hospital




Duration of stay as per Barthel Index
Barthel Index
Severe
Moderate
Mild
All
5
6
8
9
3
0
2
7
6
2
0
2
2
13
10
5
10
17
28
15
0
10
20
30
Number of Subjects
13 to 14
11 to 12
9 to 10
7 to 8
≤ 6

Duration of Stay in days	All	%	Mild	%	Moderate	%	Severe	%
≤ 6	15	20.00	10	37.04	2	11.76	3	9.68
7 to 8	28	37.33	13	48.15	6	35.29	9	29.03
9 to 10	17	22.67	2	7.41	7	41.18	8	25.81
11 to 12	10	13.33	2	7.41	2	11.76	6	19.35
13 to 14	5	6.67	0	0.00	0	0.00	5	16.13
Total	75	100	27	100	17	100	31	100

Anova

SUMMARY

Groups	*Count*	*Sum*	*Average*	*Variance*
Mild	27	197	7.296296	2.678063
Moderate	17	148	8.705882	3.345588
Severe	31	298	9.612903	6.445161

ANOVA

Source of Variation	*SS*	*df*	*MS*	*F*	*P-value*	*F crit*
Between Groups	77.83279	2	38.91639	8.85263	**0.000365**	3.123907
Within Groups	316.5139	72	4.396026			
Total	394.3467	74				

By conventional criteria the association between the study groups and duration of stay in hospital is considered to be statistically significant since $p < 0.05$.

Statistical Significance

This indicates that there is a true difference among the study groups and the difference is significant. In simple terms, by assessing the functional outcome using Barthel index in ischemic stroke patients,in mild patients category the average duration of stay in hospital was reduced significantly to 7.30 days in comparison to 8.71 days in moderate patient category and 9.61 days in severe patient category with a p-value of 0.000365 according to ANOVA test

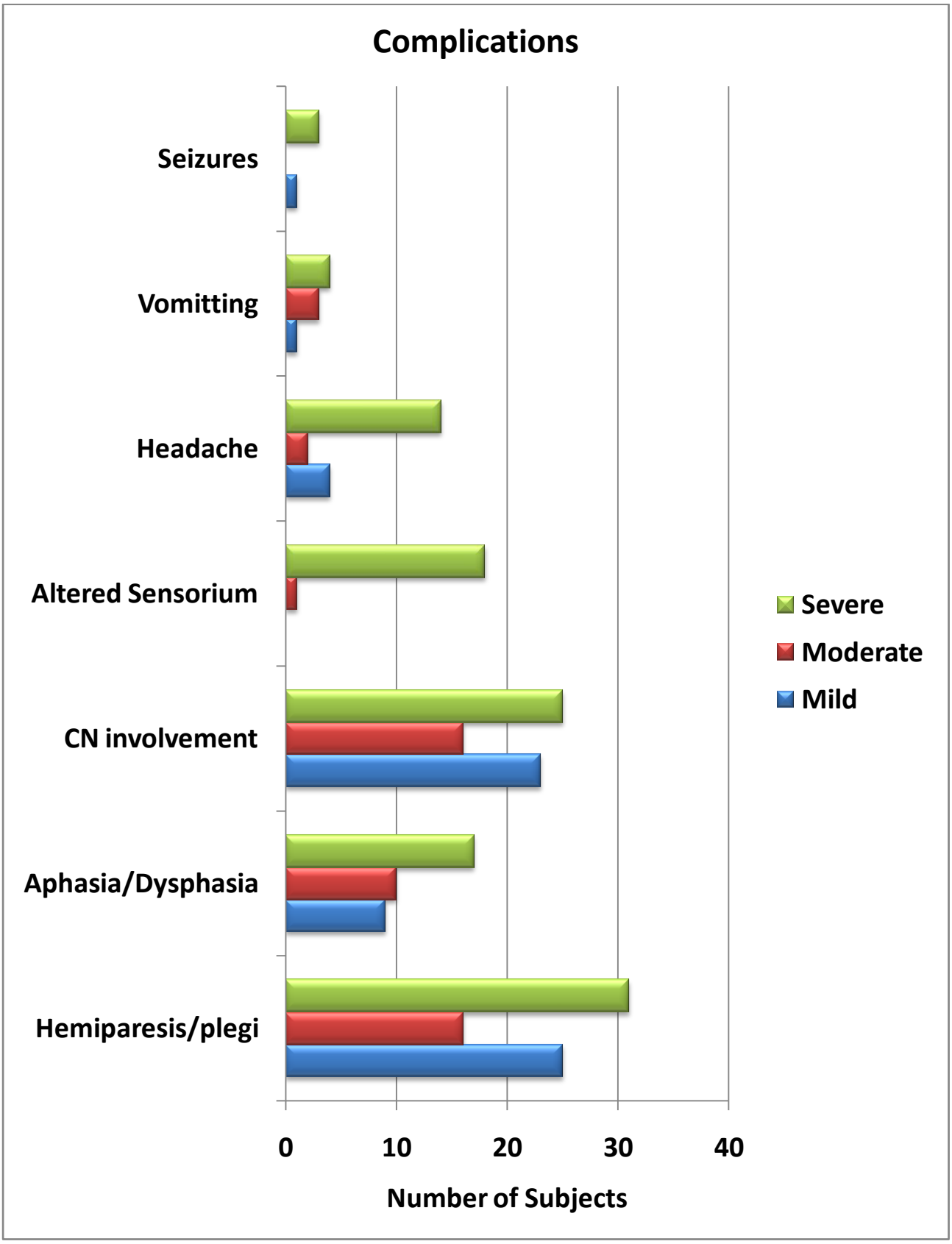
Clinical Significance

The average duration of stay in hospital by using Barthel index was meaningfully less(19.31%) inmild patients category compared to moderate patient category and also meaningfully less in moderate patient category(10.41%) compared to severe patient category. This difference is true and significant and has not occurred by chance.

Conclusion

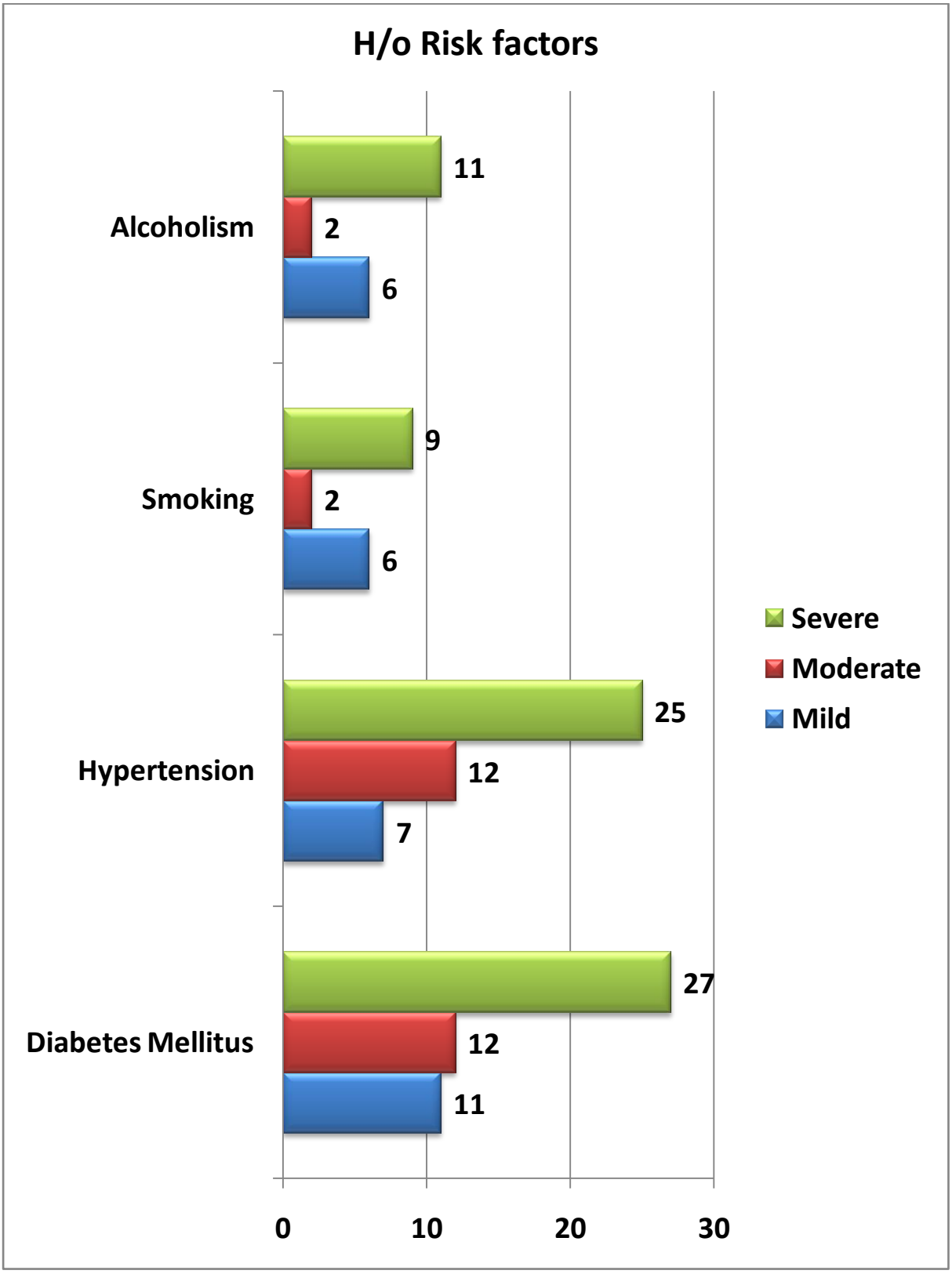
We conclude that there is real advantage if the patient is classified under mild category using Barthel index, which in turn decreases the duration of stay in hospital.

Complications



Complications	Mild	Moderate	Severe
Hemiparesis/plegia	25	16	31
Aphasia/Dysphasia	9	10	17
CN involvement	23	16	25
Altered Sensorium	0	1	18
Headache	4	2	14
Vomiting	1	3	4
Seizures	1	0	3

Risk Factors



H/o Risk Factors	Mild	Moderate	Severe
Diabetes Mellitus	11	12	27
Hypertension	7	12	25
Smoking	6	2	9
Alcoholism	6	2	11

H/o Risk Factors		Diabetes Mellitus		Hypertension		Smoking		Alcoholism	
		+	-	+	-	+	-	+	-
Mild	**27**	11	16	7	20	6	21	6	21
Moderate	**17**	12	5	12	5	2	15	2	15
Severe	**31**	27	4	25	6	9	22	11	20
Total	**75**	50	25	44	31	17	58	19	56
Chi-square		14.1		19.1		1.87		3.48	
Degrees of freedom		2		2		2		2	
P value Chi squared test without yates correction		0.003		0.000		0.392		0.175	

By conventional criteria the association between the study groups and risk factors like diabetes mellitus and hypertension is considered to be statistically significant since $p < 0.05$.

Statistical Significance

This indicates that there is a true difference among the study groups and the difference is significant.

In simple terms, by assessing the functional outcome using Barthel index in ischemic stroke patients,in mild patients category the incidence of diabetes mellitus increases significantly from 11 in mild patient category to 12 and 27 in moderate and severe patient category with a p-value of 0.003 according to Chi-Squared test.

In simple terms, by assessing the functional outcome using Barthel index in ischemic stroke patients,in mild patients category the incidence of hypertension increases significantly from 7 in mild patient category to 12 and 25 in moderate and severe patient category with a p-value of 0.000 according to Chi-Squared test.

Clinical Significance

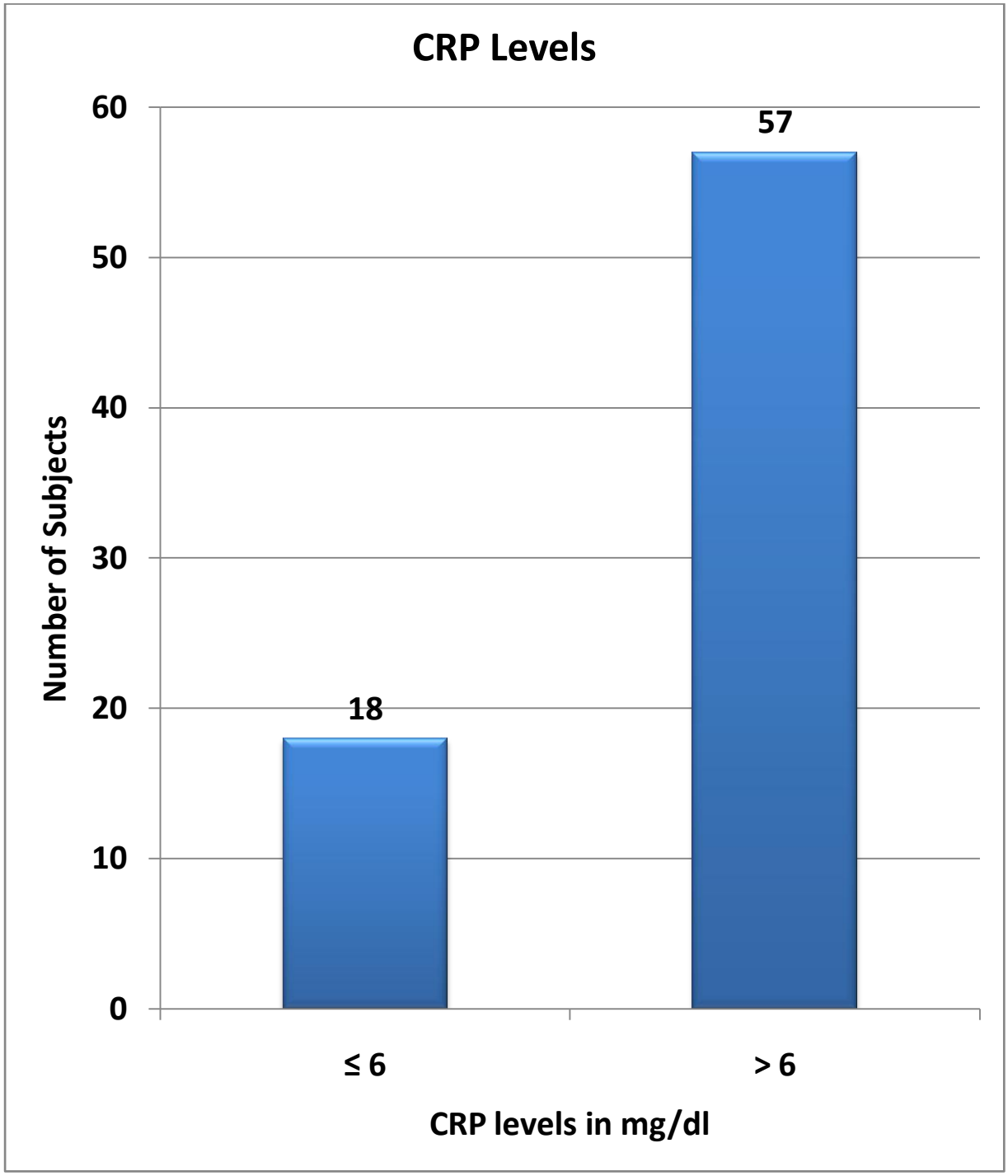
The incidence of diabetes mellitus in patients classified using Barthel index was meaningfully less(22%) in mild patients category compared to moderate patient category(24%) and severe patient category(54%). This difference is true and significant and has not occurred by chance.

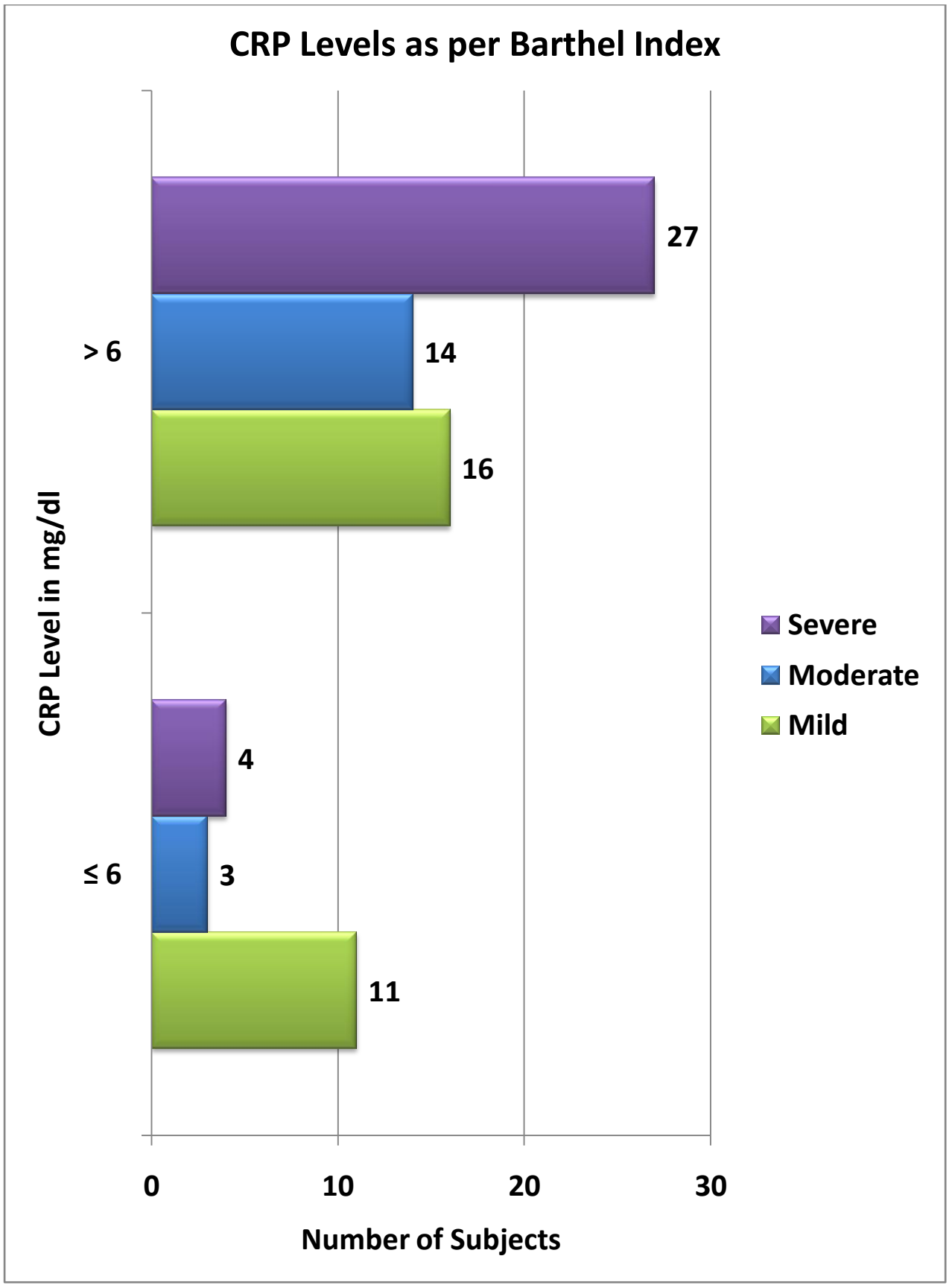
The incidence of hypertension & diabetes mellitus in patients classified using Barthel index was meaningfully less(15.91%) in mild patients category compared to moderate patient category(27.27%) and severe patient category(56.82%). This difference is true and significant and has not occurred by chance.

Conclusion

We conclude that there is real advantage if the patient is classified under mild category using Barthel index, which in turn decreases the risk of having diabetes mellitus and hypertension. This also proves there is an increasing trend of diabetes mellitus and hypertension with stroke severity.

CRP


CRP Levels
60
50
40
30
20
10
0
Number of Subjects
18
57
≤ 6
> 6
CRP levels in mg/dl


CRP Levels as per Barthel Index
CRP Level in mg/dl
> 6
≤ 6
27
14
16
4
3
11
0
10
20
30
Number of Subjects
Severe
Moderate
Mild

CRP Levels	All	%	Mild	%	Moderate	%	Severe	%
≤ 6	18	24.00	11	40.74	3	17.65	4	12.90
> 6	57	76.00	16	59.26	14	82.35	27	87.10
Total	75	100	27	100	17	100	31	100

Anova

SUMMARY

Groups	*Count*	*Sum*	*Average*	*Variance*
Mild	27	232.7	8.618518519	24.22926
Moderate	17	216.9	12.75882353	47.39632
Severe	31	560.1	18.06774194	92.78359

ANOVA

Source of Variation	*SS*	*df*	*MS*	*F*	*P-value*	*F crit*
Between Groups	1299.405808	2	649.7029038	11.21303	**0.000**	3.123907
Within Groups	4171.809659	72	57.94180082			
Total	5471.215467	74				

By conventional criteria the association between the study groups and CRP levels is considered to be statistically significant since $p < 0.05$.

Statistical Significance

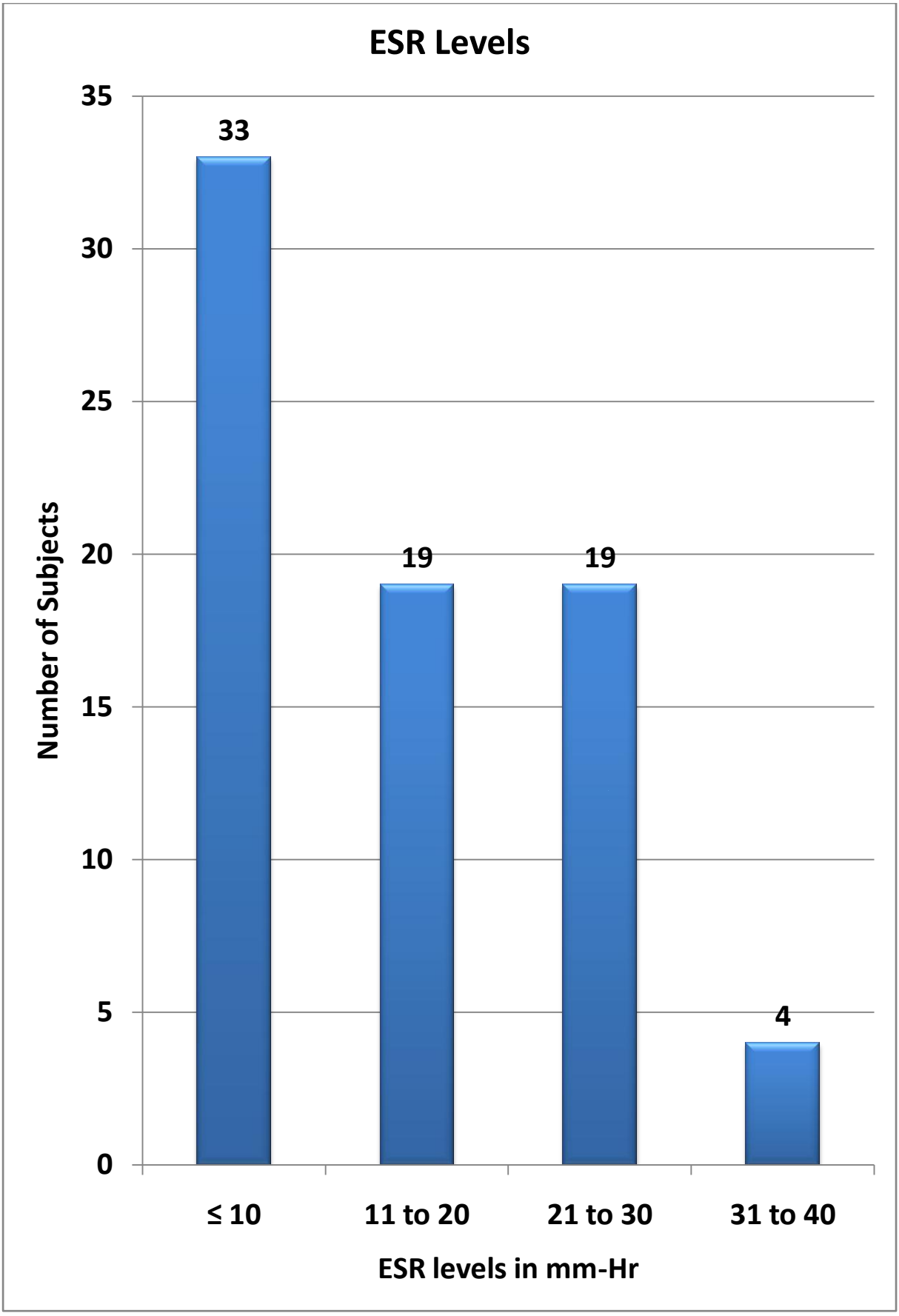
This indicates that there is a true difference among the study groups and the difference is significant. In simple terms, by assessing the functional outcome using Barthel index in ischemic stroke patients,in mild patients category the CRP levels was reduced significantly to 8.61 mg/dlin comparison to 12.75 mg/dl in moderate patient category and 18.05 mg/dl in severe patient category with a p-value of 0.000 according to ANOVA test

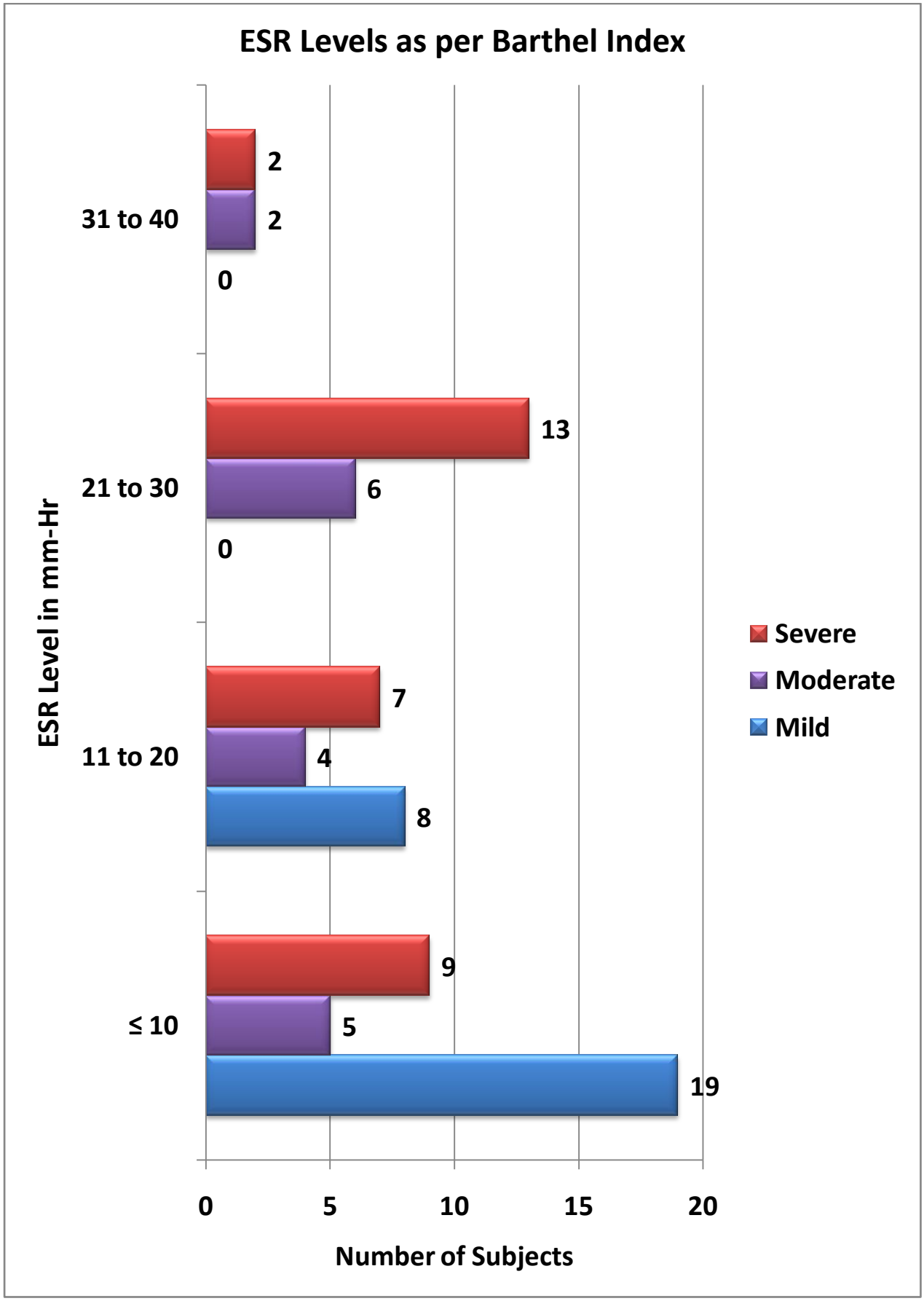
Clinical Significance

The average CRP levels >6mg/dl in patients classified using Barthel index was meaningfully less (59.26%) in mild patients category compared to moderate patient category(82.35%) compared to severe patient category(87.10%). This difference is true and significant and has not occurred by chance.

Conclusion

We conclude that there is real advantage if the patient is classified under mild category using Barthel index, which in turn is associated with decreased CRP levels. This also proves there is an increasing trend of raised CRP levels with stroke severity.


ESR Levels
35
30
25
20
15
10
5
0
Number of Subjects
33
19
19
4
≤ 10
11 to 20
21 to 30
31 to 40
ESR levels in mm-Hr


ESR Levels as per Barthel Index
ESR Level in mm-Hr
31 to 40
21 to 30
11 to 20
≤ 10
2
2
0
13
6
0
7
4
8
9
5
19
0
5
10
15
20
Number of Subjects
Severe
Moderate
Mild

ESR (mm-hr)	All	%	Mild	%	Moderate	%	Severe	%
≤ 10	33	44.00	19	70.37	5	29.41	9	29.03
11 to 20	19	25.33	8	29.63	4	23.53	7	22.58
21 to 30	19	25.33	0	0.00	6	35.29	13	41.94
31 to 40	4	5.33	0	0.00	2	11.76	2	6.45
Total	75	100	27	100	17	100	31	100

Anova

SUMMARY

Groups	*Count*	*Sum*	*Average*	*Variance*
Mild	27	259	9.592593	7.789174
Moderate	17	318	18.70588	87.84559
Severe	31	609	19.64516	91.76989

ANOVA

Source of Variation	*SS*	*df*	*MS*	*F*	*P-value*	*F crit*
Between Groups	1642.242	2	821.121	13.55624	**0.000**	3.123907
Within Groups	4361.145	72	60.57145			
Total	6003.387	74				

By conventional criteria the association between the study groups and ESR levels is considered to be statistically significant since $p < 0.05$.

Statistical Significance

This indicates that there is a true difference among the study groups and the difference is significant. In simple terms, by assessing the functional outcome using Barthel index in ischemic stroke patients,in mild patients category the ESR levels was reduced significantly to 9.59 mm -hr in comparison18.71mm -hr in moderate patient category and 19.65 mm -hr in severe patient category with a p-value of 0.000 according to ANOVA test

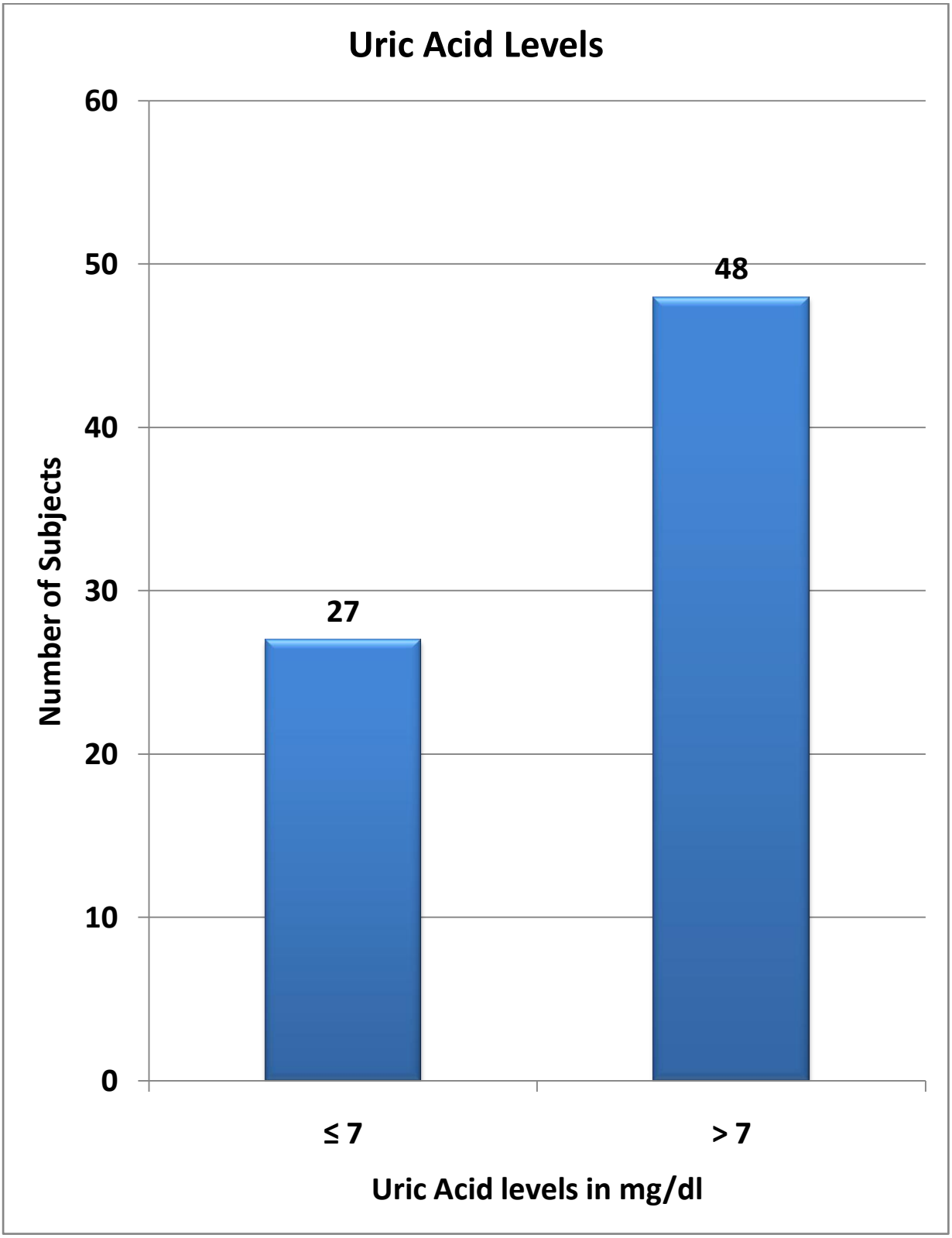
Clinical Significance

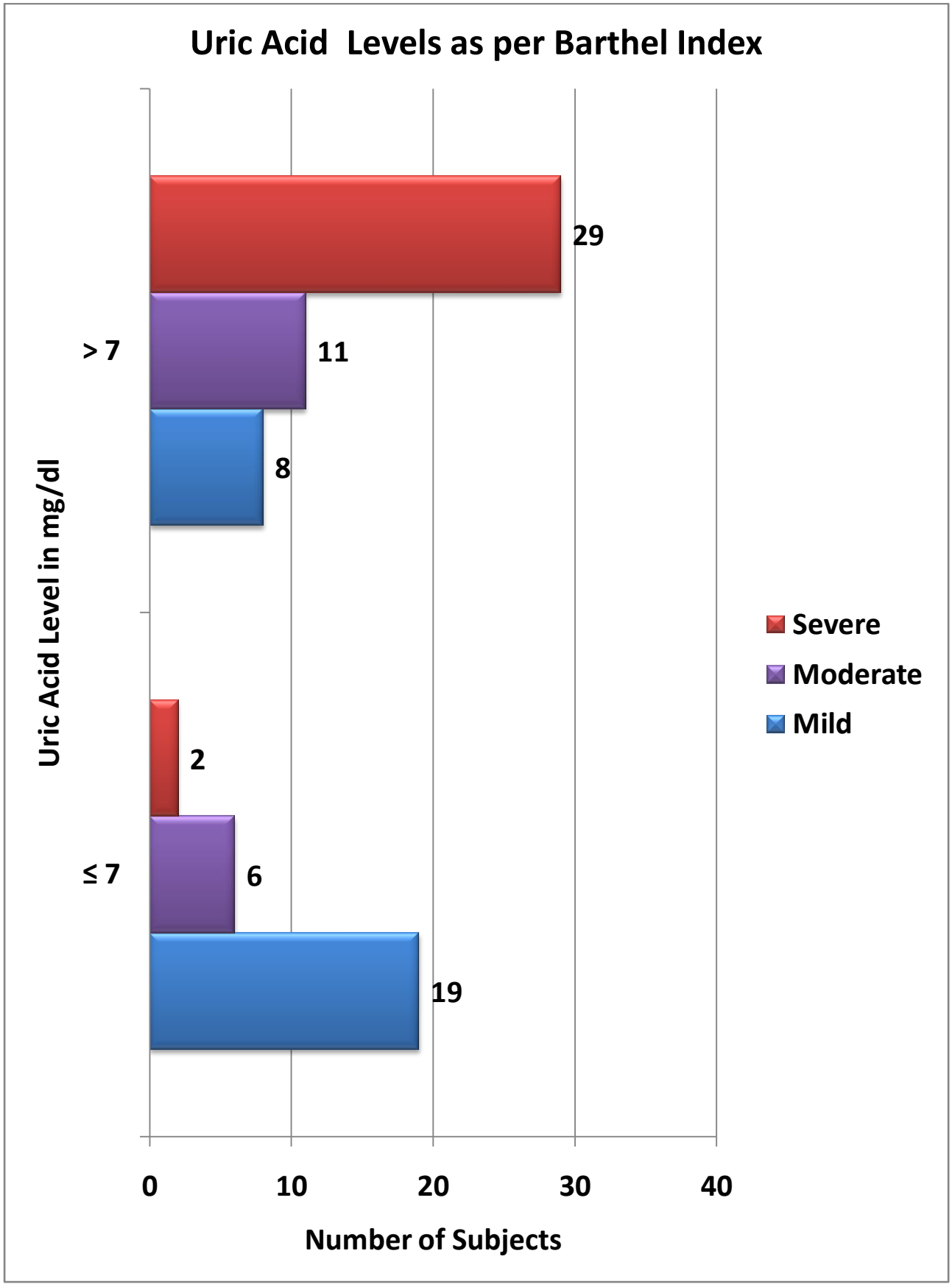
The average ESR levels in patients classified using Barthel index was meaningfully less (95%) in mild patients category compared to moderate patient category and also meaningfully less in moderate patient category(5.00%) compared to severe patient category. This difference is true and significant and has not occurred by chance.

Conclusion

We conclude that there is real advantage if the patient is classified under mild category using Barthel index, which in turn is associated with decreased ESR levels. This also proves there is an increasing trend of raised ESR levels with stroke severity.

Uric Acid


Uric Acid Levels
60
50
40
30
20
10
0
Number of Subjects
48
27
≤ 7
> 7
Uric Acid levels in mg/dl


Uric Acid Levels as per Barthel Index
Uric Acid Level in mg/dl
> 7
≤ 7
29
11
8
2
6
19
0
10
20
30
40
Number of Subjects
Severe
Moderate
Mild

Uric Acid (mg/dl)	All	%	Mild	%	Moderate	%	Severe	%
≤ 7	27	36.00	19	70.37	6	35.29	2	6.45
> 7	48	64.00	8	29.63	11	64.71	29	93.55
Total	75	100	27	100	17	100	31	100

Anova

SUMMARY

Groups	*Count*	*Sum*	*Average*	*Variance*
Mild	27	182	6.740741	8.968661
Moderate	17	153	9	7.5
Severe	31	344	11.09677	5.290323

ANOVA

Source of Variation	*SS*	*df*	*MS*	*F*	*P-value*	*F crit*
Between Groups	273.8918	2	136.9459	19.26197	**0.000**	3.123907
Within Groups	511.8949	72	7.109651			
Total	785.7867	74				

By conventional criteria the association between the study groups and uric acid levels is considered to be statistically significant since $p < 0.05$.

Statistical Significance

This indicates that there is a true difference among the study groups and the difference is significant. In simple terms, by assessing the functional outcome using Barthel index in ischemic stroke patients,in mild patients category the uric acid levels was reduced significantly to 6.74 mg/dlin comparison9.00 mg/dlin moderate patient category and 11.10md/dl in severe patient category with a p-value of 0.000 according to ANOVA test

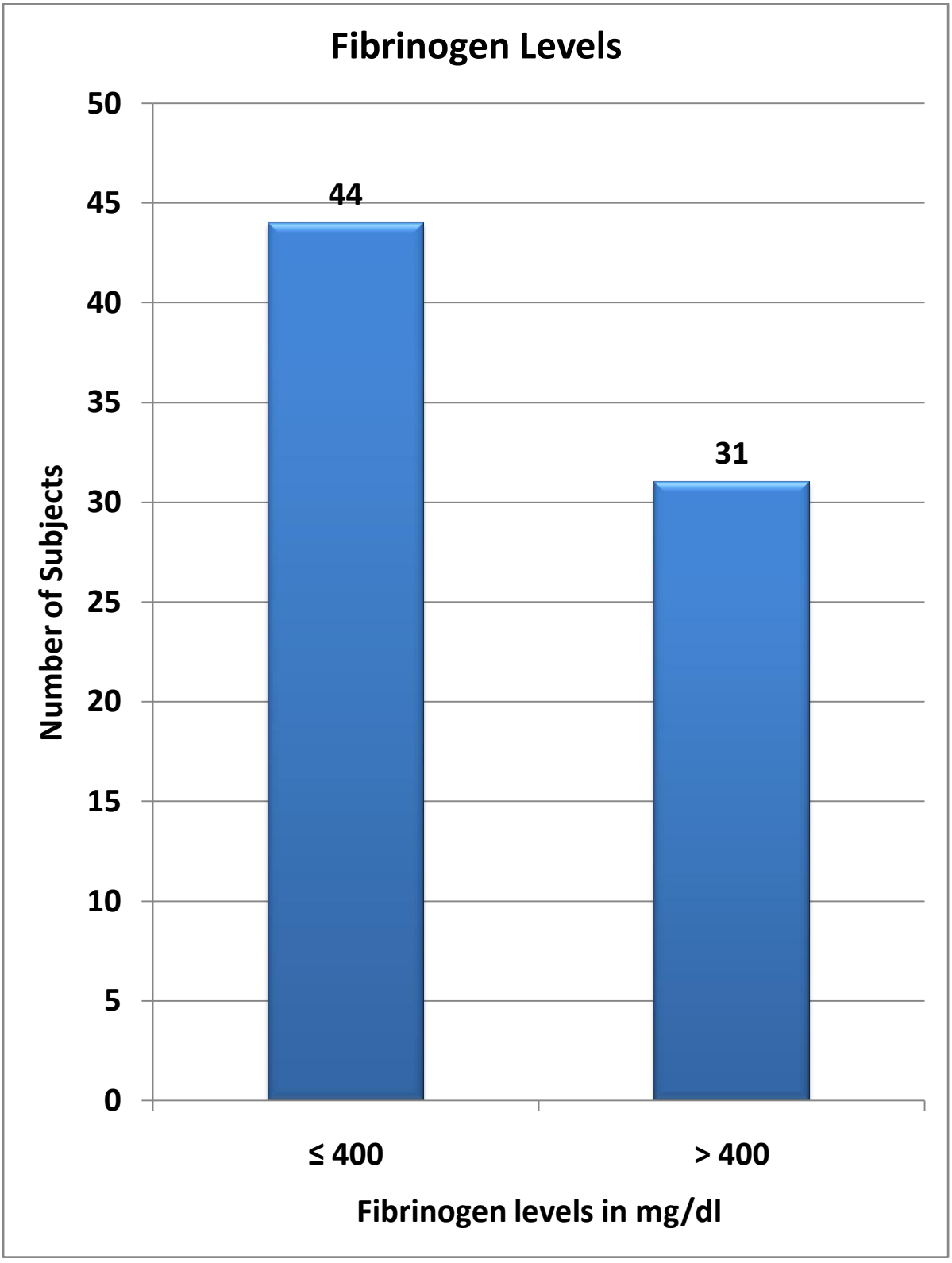
Clinical Significance

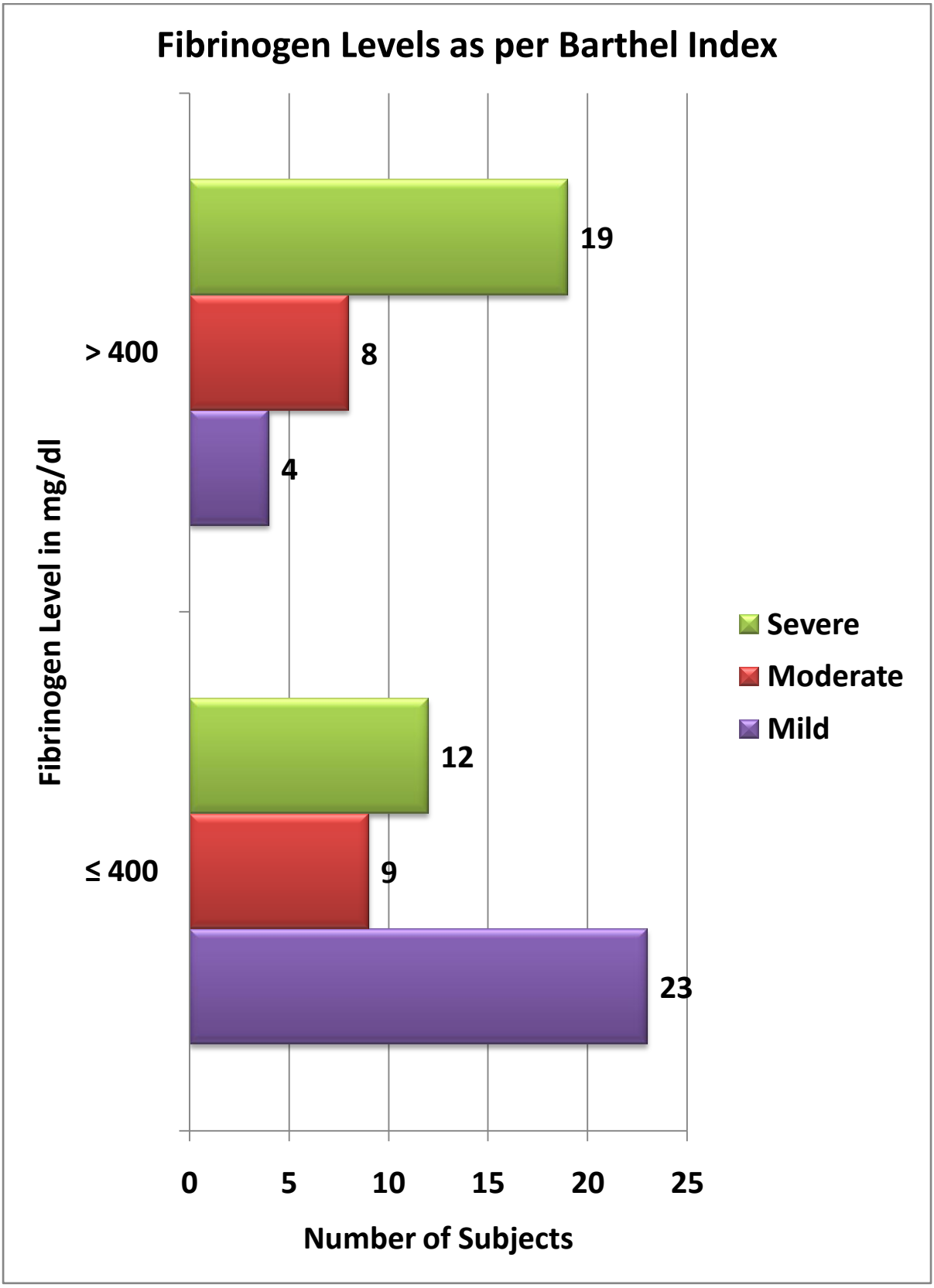
The average uric acid levels in patients classified using Barthel index was meaningfully less (33.51%) in mild patients category compared to moderate patient category and also meaningfully less in moderate patient category(23.29%) compared to severe patient category. This difference is true and significant and has not occurred by chance.

Conclusion

We conclude that there is real advantage if the patient is classified under mild category using Barthel index, which in turn is associated with decreased uric acid levels. This also proves there is an increasing trend of raised uric acidlevels with stroke severity.

Fibrinogen


Fibrinogen Levels
50
45
40
35
30
25
20
15
10
5
0
Number of Subjects
44
31
≤ 400
> 400
Fibrinogen levels in mg/dl


Fibrinogen Levels as per Barthel Index
Fibrinogen Level in mg/dl
> 400
≤ 400
19
8
4
12
9
23
Severe
Moderate
Mild
0
5
10
15
20
25
Number of Subjects

Fibrinogen (mg/dl)	All	%	Mild	%	Moderate	%	Severe	%
≤ 400	44	58.67	23	85.19	9	52.94	12	38.71
> 400	31	41.33	4	14.81	8	47.06	19	61.29
Total	75	100	27	100	17	100	31	100

Anova

SUMMARY

Groups	*Count*	*Sum*	*Average*	*Variance*
Mild	27	8794	325.7037	7284.14
Moderate	17	7043	414.2941	11233.22
Severe	31	14307	461.5161	19143.26

ANOVA

Source of Variation	*SS*	*df*	*MS*	*F*	*P-value*	*F crit*
Between Groups	269546.6	2	134773.3	10.28567	**0.000118**	3.123907
Within Groups	943416.9	72	13103.01			
Total	1212964	74				

By conventional criteria the association between the study groups and serum fibrinogen levels is considered to be statistically significant since $p < 0.05$.

Statistical Significance

This indicates that there is a true difference among the study groups and the difference is significant. In simple terms, by assessing the functional outcome using Barthel index in ischemic stroke patients,in mild patients category the fibrinogen levels was reduced significantly to 325.70 mg/dl in comparison414.29 mg/dl in moderate patient category and 461.52 md/dl in severe patient category with a p-value of 0.000118 according to ANOVA test

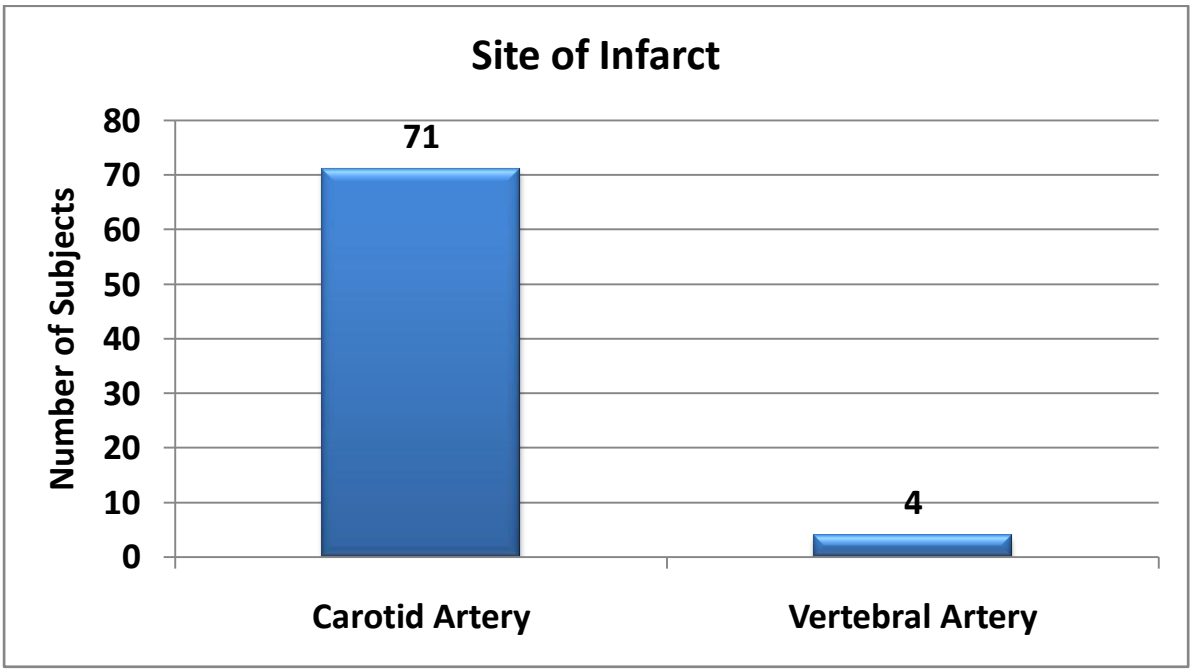
Clinical Significance

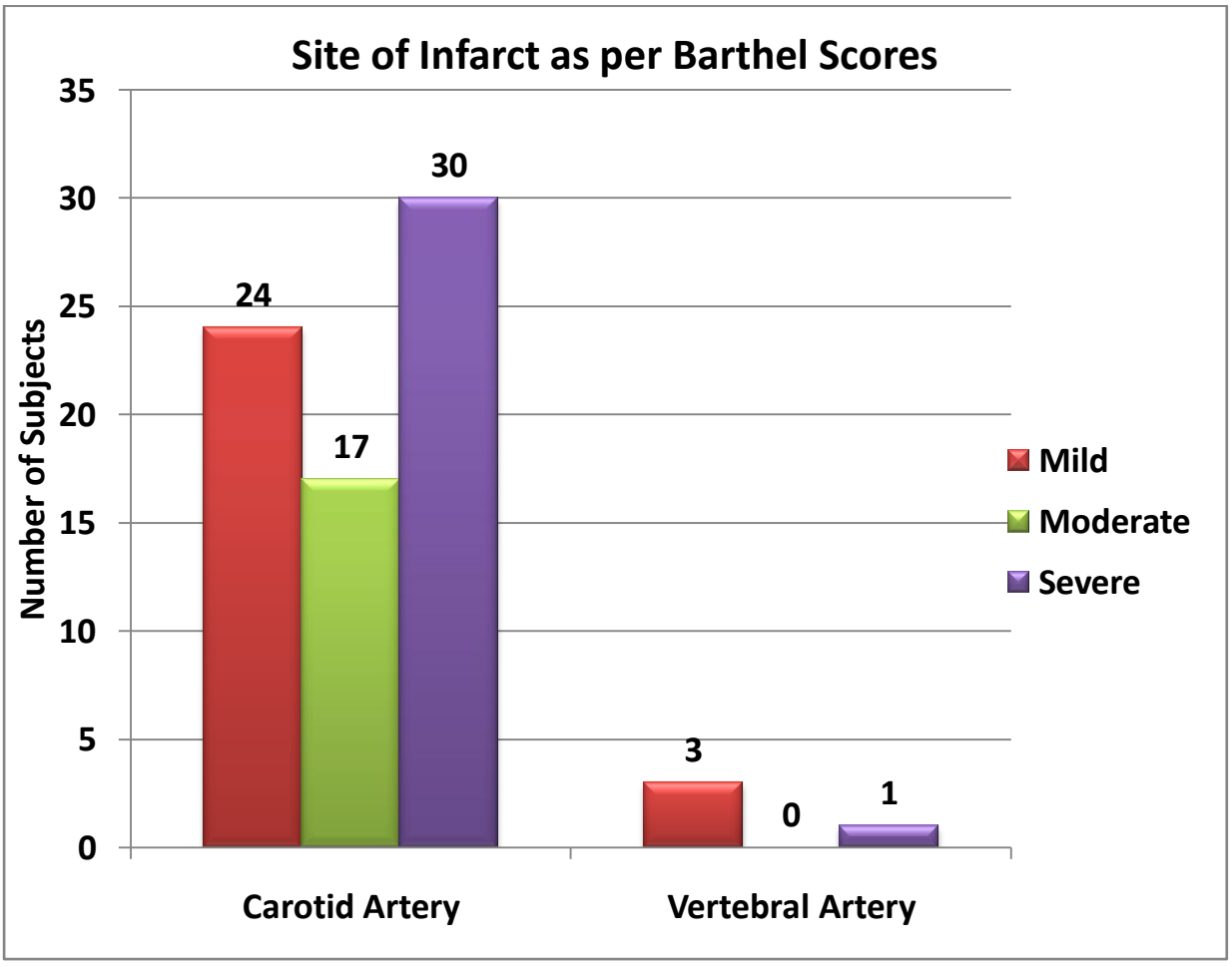
The average fibrinogen levels in patients classified using Barthel index was meaningfully less (27.20%) in mild patients category compared to moderate patient category and also meaningfully less in moderate patient category (11.40%) compared to severe patient category. This difference is true and significant and has not occurred by chance.

Conclusion

We conclude that there is real advantage if the patient is classified under mild category using Barthel index, which in turn is associated with decreased serum fibrinogen levels. This also proves there is an increasing trend of raised fibrinogen levels with stroke severity.

Site of Infarct

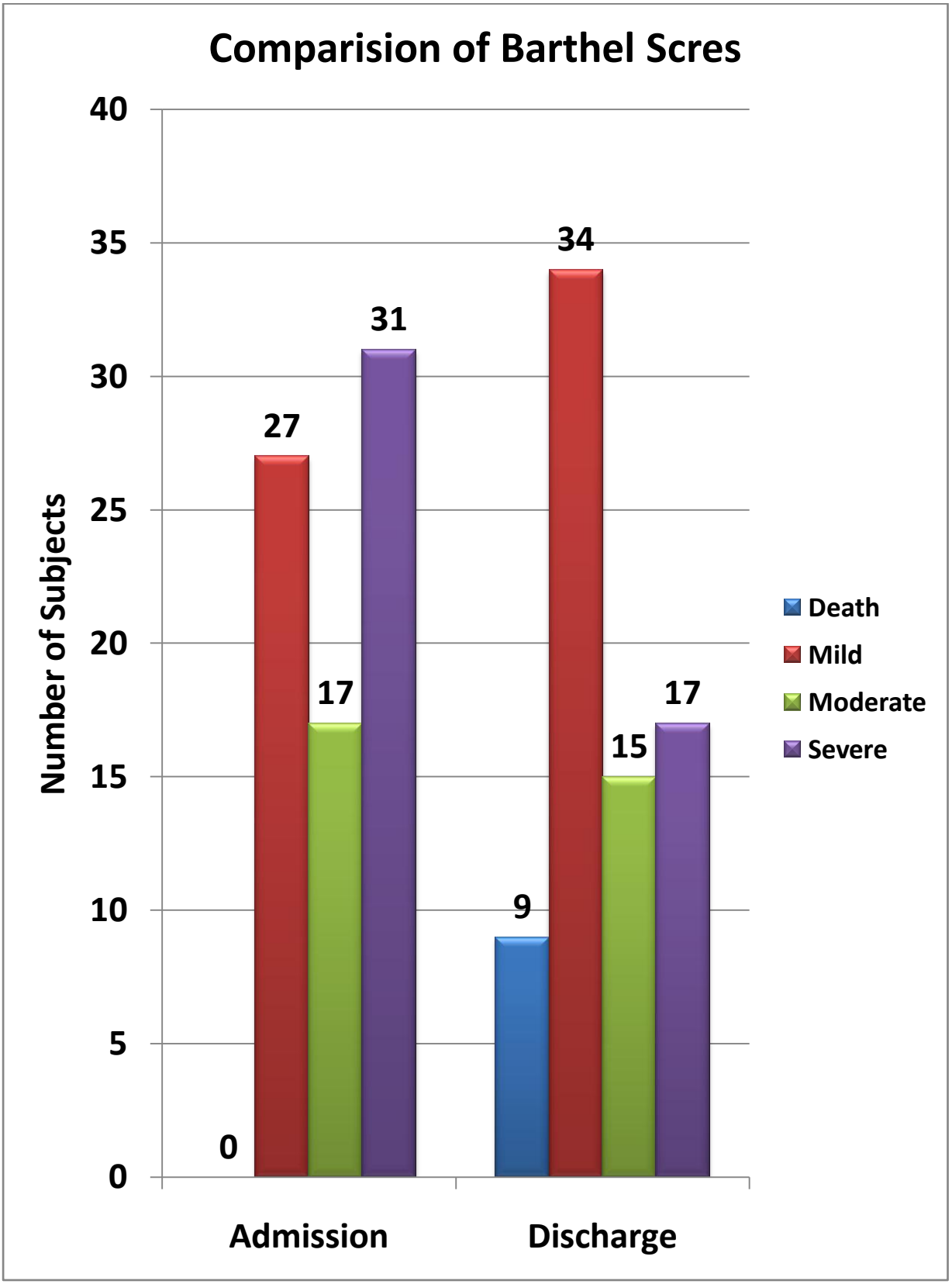




Site of Infarct	All	%	Mild	%	Moderate	%	Severe	%
Carotid Artery	71	94.67	24	88.89	17	100.00	30	96.77
Vertebral Artery	4	5.33	3	11.11	0	0.00	1	3.23
Total	75	100	27	100	17	100	31	100
Chi-square			**3.70**					
Degrees of freedom			**2**					
P value Chi squared test without yates correction			**0.157**					

By conventional criteria the association between the study groups and site of infarct is considered to be not statistically significant since $p > 0.05$.

Barthel Scores



Barthel Score	Admission	Discharge
N	**75**	**67**
Mean	**52.26667**	**56**
SD	**28.96052**	**32.93113**

Barthel Score	Admission	%	Discharge	%
Death	0	0	9	12.00
Mild	27	36	34	45.33
Moderate	17	22.66	15	20.00
Severe	31	41.33	17	22.67
Total	75	100	75	100
P Value Paired t test	**0.0000**			

In our Study 66 patients got discharged and 9 patients expired. Mortality Rate 12 %. By conventional criteria the association between the study groups and Barthel scores (Admission and Discharge) is considered to be statistically significant since $p < 0.05$.

Statistical Significance

This indicates that there is a true difference among the study groups and the difference is significant. In simple terms, by assessing the functional outcome using Barthel index in ischemic stroke patients at admission and discharge, the average Barthel score in patients at the time of admission was 52.27 in comparison to significantly increased Barthel score at discharge(56) with a p-value of 0.0000 according to paired t- test

Clinical Significance

The average Barthel scores was meaningfully less (36%) in mild patients category compared to compared to severe patient category(41.33) at admission.

The average Barthel scores was meaningfully more (45.33%) in mild patients category compared to compared to severe patient category(22.67) at discharge.

This difference is true and significant and has not occurred by chance.

Conclusion

We conclude that there is real advantage if the patient is classified using Barthel index for diagnosis and prognosis, which in turn is associated with stroke severity.

CITATIONS:

1) VK Singh et al studied the prognostic significance of CRP in ischemic stroke on 48 patients within 24 hours of ischemic stroke & at discharge and an association was examined. It showed that CRP is a better prognostic indicator of ischemic stroke at the time of discharge & has a greater utility in risk identification ($P<0.05$). Hence raised CRP values predict future outcomes in term of mortality and morbidity.

2) Medhini et al studied on patient with ischemic stroke. Method used was Chi-Sqaure and Fisher exact test. Study population was 100 patients. Conclusion was that patients with CRP < 6mg/dl suffered mild disease and had a good prognosis. Their Barthel scores improved with follow up. P value was significant. The association of CRP values at admission and its correlation with Barthel scores to assess the functional outcome of patient following ischemic stroke, suggest CRP as a good prognostic tool .Modified Barthel index is a good tool to assess the functional outcome of patients following ischemic stroke, in co-relation with CRP levels. Elevated CRP is highly sensitive, non specific and an independent risk factor for prediction of ischemic stroke.

3) Muir et al. studied 228 ischemic stroke admissions. Median follow up was 959 days. Geometric mean C - reactive protein concentration was >10.1 mg/L. It was found that survival in those with C-Reactive Protein> 10 mg/L was

significantly worse than in those with C-Reactive Protein < 10 mg/L (p 0.0009, log rank test).They concluded that C-Reactive Protein concentration is an independent predictor of survival after ischemic stroke. The single independent predictor of survival in this study was measurement of CRP within 72 hours of onset of symptoms.

4) Jaroslaw Zaremba et al studied the association between ESR and Ischemic stroke. It was observed that there was a positive correlation between ESR values and the extent of local brain damage.

5) Chamarro et al studied about early predictors of functional outcome of stroke using ESR, Study population : 208 ischemic stroke patients. Methodology was Stepwise logistic regression analysis. Conclusion was that ESR was an independent predictor of short term stroke outcome.

6) Titto et al studied Admission C – reactive protein after acute ischemic stroke and its association with stroke severity and mortality. Study population - 498 patients. Patients were followed up and it was found out that admission CRP is associated with stroke severity and long term mortality when measured at least 24 hours after onset. Hence CRP is an independent predictor of long term mortality after ischemic stroke

7) Gregory et al studied relationship between fibrinogen levels and functional outcome from acute ischemic stroke. Method of study was Multiple Logistic regression analysis. Placebo data from the Stroke treatment with Ancrod Trial

(STAT) and European stroke treatment with Ancrod trial (ESAT) were analysed. In both univariate & multivariate analysis the proportion of patients with good functional outcome decreased with increasing quartiles of initial fibrinogen levels in both groups. Patient with initial fibrinogen levels < 450 mg/dl had a better outcome.

8) Arnon et al studied the inflammatory response in the first 48 hours of acute ischemic Stroke .Study duration 2005-2007. They concluded that significant increase in inflammatory substance in the first few days have an important role in ischemic brain injury and can affect the short as well as long term clinical outcome.

9) William whitely et al from UK conducted a study to determine whether markers of inflammation (White cell count, CRP and fibrinogen are associated with a poor outcome after stroke. Study type Prospective study. Duration 2002-2005.Population size – 844 .Confidence intervals were significant for these variables. Hence it concluded that raised levels of markers after stroke are associated with poor outcomes.

10) Angel Chamorre et all study had a population of 881 patients with Acute ischemic stroke and found the association between functional outcome of stroke and uric acid measured at hospital admission. Method of study: logistic regression. In patients with acute ischemic stroke, there is a 12% increase in the

Odds of good clinical outcome for each milligram per decilitre increase of serum uric acid. This finding reinforces the relevance of oxidative damage in ischemic stroke.

11) H.J Milionis et al from UK studied in 163 patients for Serum uric acid levels and risk for acute ischemic non-embolic stroke in elderly subjects. It was a case–control study done in Greece. The association between SUA and stroke was determined by multivariate logistic regression modelling after adjusting for potential confounding factor. Elevated SUA is associated with an increased risk for acute ischemic/non-embolic stroke in a strictly defined population of elderly individuals independently of concurrent metabolic derangements.($P<0.05$).

CONCLUSION:

CRP apart from being an inflammatory marker has also been found to be a highly sensitive, non specific and an independent risk factor for prediction of Ischemic stroke. Similarly ESR, fibrinogen, Uric acid have also been found to be useful as early indicator of prognosis in Stroke patients.

The present study is done without any haste involving the above four parameters to predict the outcome among stroke patients. This study correlates with the previous studies done by eminent people as quoted by my citations

Inclusion of these tests in patients with acute stroke provides clinicians with a low cost and useful way to predict functional outcome after ischemic stroke, as measured by Barthel index which has been proved to have a strong correlation with inflammatory markers.

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PROFORMA

PRELIMINARY DATA OF THE PATIENT

Name: **Age**: **Sex**: **IP NO:**

Address: **PH No:**

DOA: **DOD:**

Occupation: **Income**: **Religion**:

CONSENT

I ---------- , unreservedly and in my full sense give my consent to take part in this study, the risks and benefits of which have been explained to me in my vernacular language

CHIEF complaints:

1) Weakness : UL
LL Present/absent Present/absent
Face

Since-----

2) Deviation of mouth: Present/absent: to left/right Since------

3) Altered level of consciousness Present/absent Since------

PRESENTING COMPLAINTS:

According to the patients /attenders words		**Right**	**Left**
Weakness:	UL		
	LL	Present/absent	Present/absent
	Face		

Onset: Sudden /gradual /progression- over min /hours/days
During activity /at rest/during sleep

Prodromal Symptoms:
Headache within 2hrs of onset of weakness/giddiness/vertigo/vomiting: Present/absent

H/o convulsions: Present/absent: If present: focal /generalised

H/o of loss of consciousness: Present/absent
Duration of altered State:
Onset: Sudden /gradual
Deteriorating/Recovering

Other symptoms:
Bladder Bowel disturbance: Present/absent
Involuntary movements: Present/absent
Inability to speak/ altered speech: Present/absent

H/o of cranial nerve involvement: H/o of loss of vision/ diplopia /change in voice/nasal regurgitation: Present/absent
H/o of swaying present/absent
H/o sensory disturbances: Present/absent
H/o trauma (head): Present/absent
H/o Chest pain /palpitation/dyspnoea/PND/orthopnoea
H/o of joint pain /fever

PAST MEDICAL HISTORY

Diabetes Mellitus / Hypertension / Intermittent Claudication/ TIA / VBI / Stroke/ Heart disease- IHD, RHD/ Trauma to head and spine/ Bleeding Diathesis/ Syphilis/ TB/ Migraine /Seizures/Gout : - YES/NO

Surgical history if any:

Drug Intake: OCP/Anticoagulants/Cocaine/amphetamine/others

FAMILY HISTORY: Hx of similar complaints/ stroke/ hypertension/ Sudden Death/ DM/ IHD/ Hyper-coagulable states.

PERSONAL HISTORY
Diet:Veg /Non Veg ;
Smoking – Average no of Beedies /cigarettes smoked per day /no of years. Smoking index
Appetite: Good /poor
Sleep: Sound /disturbed
Alcohol intake:

a) Yes/No
b) If yes - No of years, Nature of drink (brand)
c) Amount consumed per day (Avg) Alcohol index ml/day *Duration in years
d) Stopped??

Bowel and Bladder: Regular/altered
Illicit drugs : Yes /No
Marital status: married /unmarried
Menstrual history if any: Age of menarche / menopause; Regular /irregular cycles

Treatment history: if any

GENERAL PHYSICAL EXAMINATION
Built & Nourishment: Height in cm; Weight in Kg; BMI kg/m2
Pallor / Cyanosis /Clubbing / Oedema / Icterus / Lymphadenopathy / edema
Carotid Bruit
Evidence of any congenital abnormalities

VITAL PARAMETERS
Pulse: Rate /Rhythm/Volume/Character/All peripheral pulses/ RR –RF delay/
Condition of the vessel wall: Bruit Thrill.
Peripheral pulses:
BP:in mmHG :

Supine	Standing	Standing

Right UL: Left UL: Right UL: Left UL: Right LL:
RR: .../min
JVP:
Temperature: in degree Celsius

Neurocutaneous markers: Yes/No

Skull /Spine:

Thyroid/Breast:

SYSTEMIC EXAMINATION

A.CENTRAL NERVOUS SYSTEM

Handedness: Right /Left

HMF

Consciousness: Alert /drowsy/stuporous/comatose
If alert
Orientation: Time/place/person: present /absent
Memory: Intact/Lost
Speech and language: Normal/aphasic/dysarthric

B**. Cranial nerves:**

1. Olfactory (sense of smell-preserved/altered/lost)

Right Left

2. Optic: Visual acuity- normal /reduced
   Field of vision – normal /reduced
   Colour vision – normal /altered
   Fundus : normal/abnormal

3/4/6.Oculomotor, Trochlear, Abducent
   Eye movement –individual &conjugate – full range /restricted
   Nystagmus: present /absent
   Squint: present /absent
   Ptosis: present /absent

	RIGHT	LEFT
Pupils' size:		
Light Reflex		
Accommodation Reflex		

5. Trigeminal (Sensation of face jaw and motor):
   MOTOR
   Sensory
   Secretory
   Reflexes: corneal /conjunctival/jaw jerks
7. Facial (motor, taste anterior 2/3 of tongue, stapedial reflex, lacrimation)
8. Vestibulocochlear nerve (Rinnes and Webers)
9. Glossophayngeal and 10.Vagal (uvula position, palatal movement, gag reflex or pharyngeal reflex)
11. Accessory (SCM and trapezius)
12. Hypoglossal (tongue wasting fasciculations, deviation, power)

C.Motor System

1. Bulk: wasting /atrophy measure UL and LL
2. Tone: normal/hypo/hyper
3. Power MRC scale 0-5

Neck
- Flexors
- Extensors

	RIGHT	LEFT
UL		
Shoulder		
Flexion		
Extension		
Abduction		
Adduction		
Elbow		
Flexion		
Extension		
Wrist		
Flexion		
Extension		
Hand Grip		
Lower Limbs:		
Hip		
Flexion		
Extension		
Abduction		
Adduction		
Knee		
Flexion		
Extension		
Ankle		
Dorsi-Flexion		
Plantar Flexion		
Inversion		
Eversion		
Toe Grip		

4. Co-ordination:

Upper Limbs:
- Finger nose & Finger Finger Nose Test
- Dysdiadokinesia

Lower limbs
- Heel knee test
- Tandam walking
- Rhombergs Test

Other cerebellar Signs:
- Dysmetria

Rebound phenomenon
Pendular knee jerk
Nystagmus
Scanning speech

5. Involuntary movements:
6. Gait:

D. Sensory System:

Touch — Affected or not affected
Pain
Temperature
Position Sense
Vibration sense
Cortical sensation
Graphaesthesia
Stereognosis

Tactile Localisation
Sensory inattention

E.Reflexes

1. Superficial
   A) Corneal
   B) Conjunctival
   C) Pharyngeal (gag)
   D) Abdominal: Upper and lower
   E) Cremastric
   F) Plantar

2. DTR:

	BICEPS	TRICEPS	SUPINATOR	FINGERFLEXOR	KNEE	ANKLE
Right						
Left						

Other: Jaw jerk /Hoffmans sign – R/L

Clonus: Ankle and patellar

3. Primitive Reflexes : present /absent.
   Glabellar tap/ palmomental/ Snout/ Sucking/ Grasp reflexes
4. Visceral reflexes – Bulbo-cavernous and anal reflex

F. Meningeal Signs:

RESPIRATORY SYSTEM:

Respiratory Rate: Rhythm
Any features suggestive of Aspiration Pneumonia:

CVS:

ABDOMEN:

<u>INVESTIGATIONS</u>:
Blood:
Hb%
TC, DC

Bl Urea:
S.Creatinine:

RBS/ FBS / PPBS

S Electrolytes : Na K

Urine Routine Examination: Albumin Sugar deposits

CXR-PA View:

ECG:

Fasting Lipid Profile:
TC:
LDL:
HDL:
VLDL:
TG:

ESR:

Serum CRP:

Serum Uric Acid

Plasma Fibrinogen

2D – ECHO

CT scan Brain: - Infarct Region- Infarct size-

PROVISIONAL / CLINICAL DIAGNOSIS:

TREATMENT GIVEN:

Date of Discharge / Death:

STATUS AT DISCHARGE: ----------

THE BARTHEL INDEX

Patient Name: _____ **Rater Name: _____Date: _____**

Activity Score

FEEDING_____

0 = unable

5 = needs help cutting, spreading butter, etc., or requires modified diet

10 = independent

BATHING_____

0 = dependent

5 = independent (or in shower)

GROOMING_____

0 = needs to help with personal care

5 = independent face/hair/teeth/shaving (implements provided)

DRESSING_____

0 = dependent

5 = needs help but can do about half unaided

10 = independent (including buttons, zips, laces, etc.)

BOWELS_____

0 = incontinent (or needs to be given enemas)

5 = occasional accident

10 = continent

BLADDER_____

0 = incontinent, or catheterized and unable to manage alone

5 = occasional accident

10 = continent

TOILET USE_____

0 = dependent

5 = needs some help, but can do something alone

10 = independent (on and off, dressing, wiping)

TRANSFERS (BED TO CHAIR AND BACK) _____

0 = unable, no sitting balance

5 = major help (one or two people, physical), can sit

10 = minor help (verbal or physical)

15 = independent

MOBILITY (ON LEVEL SURFACES) _____

0 = immobile or < 50 yards

5 = wheelchair independent, including corners, > 50 yards

10 = walks with help of one person (verbal or physical) > 50 yards

15 = independent (but may use any aid; for example, stick) > 50 yards

STAIRS _____

0 = unable

5 = needs help (verbal, physical, carrying aid)

10 = independent

TOTAL (0–100): _____

GOVT. STANLEY MEDICAL COLLEGE, CHENNAI – 600001

INFORMED CONSENT

A STUDY ON BIOCHEMICAL PARAMETERS ESR,CRP, URIC ACID AND FIBRINOGEN FOR PREDICTION OF FUNCTIONAL OUTCOME IN PATIENTS WITH ISCHEMIC STROKE AT GOVERNMENT STANLEY HOSPITAL, CHENNAI.

Place of study: govt. Stanley medical college, Chennai

I ……. have been informed about the details of the study in my own language.

I have completely understood the details of the study.

I am aware of the possible risks and benefits, while taking part in the study.

I understand that I can withdraw from the study at any point of time and even then, I can receive the medical treatment as usual.

I understand that I will not get any money for taking part in the study.

I will not object if the results of this study are getting published in any medical journal, provided my personal identity is not revealed.

I know what I am supposed to do by taking part in this study and I assure that I would extend my full cooperation for this study.

Volunteer:	Witness:
Name and address	Name and address
Signature/thumb impression:	Signature/thumb impression
Date:	Date:

Investigator

Signature and date

இரத்த நாளங்களின் அடைப்பினால் பக்கவாதம் ஏற்பட்டு அரசாங்க ஸ்டான்லி மருத்துவமனைக்கு வரும் நோயாளிகளின் இரத்த சிஆர்பி இஎஸ்ஆர் யூரிக் ஆஸிட் பைபிரினோஜன் என்னும் பரிசோதணை மூலம் அவர்களின் செயல்பாட்டு விளைவினை கண்டறிய ஒரு ஆய்வு

ஆய்வாளர்:**மரு.வினோத் குமார்**,

முதுநிலைபட்டமேற்படிப்புமாணவர்,

பொதுமருத்துவ பட்டபடிப்பு.

வழிகாட்டி : **பேராசிரியர் மரு. வசுமதி ஜீ**,

பொதுமருத்துவபேராசிரியர்,

அரசுஸ்டான்லிமருத்துவமனை.

<u>சுயஒப்புதல்படிவம்</u>

பெயர்: வயது: உள்ளிருப்புஎண்:

இந்த மருத்துவ ஆய்வின் விவரங்கள் எனக்கு விளக்கப்பட்டது . என்னுடைய சந்தேகங்களைக்கேட்கவும்,அதற்கான தகுந்தவிளக்கங்களைப்பெறவும் வாய்ப்பளிக்கப்பட்டது .

நான் இவ்வாய்வில் தன்னிச்சையாகத்தான் பங்கேற்கிறேன் . எந்த காரணத்தினாலும் ,எந்தகட்டத்திலும், எந்த சட்டசிக்கலும் இன்றி இந்த ஆய்விலிருந்து விலகிக்கொள்ளலாம் என்றும் அறிந்துகொண்டேன் .

நான் ஆய்விலிருந்து விலகிக்கொண்டாலும் ஆய்வாளர் என்னுடைய மருத்துவ அறிக்கைகளைப்பார்ப்பதற்கோ அல்லது உபயோகிக்கவோ என் அனுமதி தேவையில்லை எனவும் அறிந்துகொண்டேன்.என்னைப்பற்றிய தகவல்கள் இரகசியமாகப்பாதுகாக்கப்படும் என்பதையும் அறிவேன்.

இந்த ஆய்வின் மூலம் கிடைக்கும் தகவல்களையும் பரிசோதனை முடிவுகளையும் .ஆய்வாளர் அவர் விருப்பத்திற்கேற்ப எவ்விதமாகப்பயன்படுத்திக்கொள்ளவும் , அதனைபிரசுரிக்கவும் முழுமனதுடன் சம்மதிக்கிறேன்.

இந்த ஆய்வில் பங்கு கொள்ள ஒப்புக்கொள்கிறேன் . எனக்குகொடுக்கப்பட்ட அறிவுரைகளின்படி நடந்துகொள்வதுடன், ஆய்வாளருக்கு உண்மையுடன் இருப்பேன் என்றும் உறுதியளிக்கிறேன் .என் உடல்நலம் பாதிக்கப்பட்டாலோ அல்லது வழக்கத்திற்கு மாறானநோய்க்குறிதென்பட்டாலோ உடனே அதை தெரிவிப்பேன் என உறுதிகூறுகிறேன் .

இந்த ஆய்வில் எனக்கு எவ்விதமான பரிசோதனைகளையும் , சிகிச்சைகளையும் மேற்கொள்ள நான் முழுமனதுடன் சம்மதிக்கிறேன் .

இப்படிக்கு

நோயளியின் கையொப்பம் ஆய்வாளர்கை யொப்பம்/பெயர்

(பெயர்:) (மரு. **வினோத் குமார்**.)

இரத்த நாளங்களின் அடைப்பினால் பக்கவாதம் ஏற்பட்டு அரசாங்க ஸ்டான்லி மருத்துவமனைக்கு வரும் நோயாளிகளின் இரத்த சிஆர்பி இஎஸ்ஆர் யூரிக் ஆஸிட் பைபிரினோஜன் என்னும் பரிசோதணை மூலம் அவர்களின் செயல்பாட்டு விளைவினை கண்டறிய ஒரு ஆய்வு

ஆய்வாளர்:**மரு.வினோத் குமார்**,

முதுநிலைபட்டமேற்படிப்புமாணவர்,

பொதுமருத்துவ பட்டபடிப்பு.

வழிகாட்டி : **பேராசிரியர் மரு. வசுமதி ஜீ**,

பொதுமருத்துவபேராசிரியர்,

அரசுஸ்டான்லிமருத்துவமனை.

<u>பங்கேற்பாளரின் தகவல் படிவம்</u>

நீங்கள் இந்த ஆய்வில் பங்கேற்க அழைக்கப்படுகிறீர்கள் . இந்த ஆய்வில் பங்கேற்கும்முன், இதன் நோக்கத்தையும், முறைகளையும் ,இதனால் ஏற்படும் பின்விளைவுகளையும் நீங்கள் அறிந்து கொள்ள ஆய்வாளர் அளிக்கும் தகவல்:

உங்கள் நோயின் வரலாறும், உங்களின் முழு உடல்பரிசோதனையும் தெளிவாகவும் விரிவாகவும் பதிவுசெய்யப்படும்.

இந்த ஆய்வின் முடிவுகள் மருத்துவ காரணங்களுக்காகவும் , மருத்துவ கல்விக்காகவும் பயன்படுத்தப்படும். இந்த ஆய்வு பற்றிய சந்தேகங்களுக்கு உரிய முறையில் விளக்கமளிக்கப்படும் . தங்களைப்பற்றிய தகவல்கள் இரகசியமாக பாதுகாக்கப்படும் .

இந்த ஆய்வில் இருந்து எப்போது வேண்டுமானாலும் தாங்கள் எவ்வித முன்னறிவிப்பின்றியும் , எவ்வித சட்டசிக்கலும் இன்றி விலகிக்கொள்ளலாம் .

இந்த ஆய்வில் பங்கேற்குமாறு கேட்டுக்கொள்கிறேன் .

நன்றி,

ஆய்வாளர் கையொப்பம் நோயாளியின் கையொப்பம்

(மரு. **வினோத் குமார்**) (பெயர்:)

INSTITUTIONAL ETHICAL COMMITTEE,
STANLEY MEDICAL COLLEGE, CHENNAI-1

Title of the Work	: A Study on Biochemical Parameters ESR, CRP, URIC ACID and Fibrinogen for prediction of functional outcome in Patients with Ischemic Stroke at Govt. Stanley Hospital, Chennai.
Principal Investigator	: Dr. VINOD KUMAR R
Designation	: P.G in M.D (General Medicine)
Department	: General Medicine

The request for an approval from the Institutional Ethical committee (IEC) was considered on the IEC meeting held on 07.04.2014 at the Council Hall, Stanley Medical College, Chennai 1 at 2 PM

The members of the Committee, the secretary and the Chairman are please to approve the proposed work mentioned above, submitted by the principal investigator.

The Principal Investigator and their team are directed to adhere to the guidelines given below:

1. You should inform the IEC in case of changes in study procedure, site investigator investigation or guide or any other changes.

2. You should not deviate from the area of work for which you applied ethical clearance.

3. You should inform the IEC immediately in case of any adverse events or serious adverse reactions

4. You should abide to the rules and regulations of the institution.

5. You should complete the work within the specified period and if any extension of time is required, you should apply for permission again and do the work

6. You should submit the summary of work to the ethical committee on completion of the work.

K Vasantha

MEMBER SECRETARY,
IEC, SMC, CHENNAI

MASTER CHART

SLN	Age	Sex	Duration stay	Symptom	DM	HTN	SMOKE	Ethanol
1	39	M	10	1,3	-	+	-	-
2	70	M	5	1,3	+	-	+	-
3	33	M	8	1,3,v	-	-	-	+
4	65	M	7	1,2,3,h	+	+	+	+
5	62	M	14	1,2,3,4h	+	+	+	+
6	40	M	10	1,3	-	+	+	-
7	52	M	6	1,3	-	-	-	-
8	48	M	8	1,3,S	-	-	+	+
9	51	M	6	1,h	+	-	+	-
10	55	M	9	1,2,3,	+	+	-	-
11	62	M	5	1,3	-	-	-	-
12	58	M	10	1,2,3,s	+	+	+	+
13	56	F	6	2,h	+	-	-	+
14	60	F	8	1,2,3,	-	-	-	-
15	72	F	7	2	+	-	-	-
16	77	F	11	1,4,v	+	+	-	-
17	70	F	9	1,3,h	+	+	-	-
18	47	F	7	1,2,s	+	+	-	-
19	49	F	8	1,3,v	+	+	-	-
20	42	M	9	1,4,v	+	-	+	-
21	52	M	7	1,2,h	+	+	+	-
22	55	M	9	1,3,h	+	+	+	+
23	80	F	10	1,3,v,h	+	-	-	-
24	63	M	11	1,2,3,h	+	+	-	-
25	75	F	12	1,4,h	+	+	-	-
26	51	M	8	1,3,v	+	-	+	+
27	45	M	7	1,2,3,h	+	+	-	-
28	63	F	13	1,3,h	+	-	-	+
29	55	F	6	1,4,h	+	+	-	-
30	54	F	12	1,3,h	+	-	-	-
31	74	F	10	1,2,3,v	+	-	-	-
32	50	F	8	1,2,3,	-	-	-	-
33	49	F	5	2	-	-	-	-
34	72	F	6	1,2,3	+	+	-	-
35	60	F	10	1,2,3,4,h,s	+	+	-	+
36	47	F	11	1,2,3	+	+	-	-
37	48	M	7	1,3	-	-	+	+
38	44	M	14	1,2,3,h	-	+	-	-
39	38	M	6	1,3,	-	-	+	-
40	39	M	8	1,3,	-	-	+	+
41	80	M	6	1,2,3	+	+	+	+
42	46	M	7	1,2,3,	+	-	-	-
43	40	M	12	1,2,3,4,h,v	-	-	+	+

MASTER CHART

SLN	Age	Sex	Duration stay	Symptom	DM	HTN	SMOKE	Ethanol
44	70	F	10	1,2,3,h	+	+	-	-
45	56	M	7	1,3	+	-	+	-
46	54	M	6	1,2,3	+	+	+	-
47	58	F	10	1,3,4	+	+	-	-
48	76	F	11	1,3	+	+	-	-
49	65	F	12	1,3,4	+	+	-	-
50	61	M	8	1,3	+	+	+	-
51	80	F	7	1,3,	+	+	-	-
52	68	M	8	1,3	+	+	-	+
53	50	M	6	1,3	-	-	+	-
54	55	M	9	1,2,3	-	-	+	-
55	48	M	11	1,2,3	-	-	-	-
56	56	M	12	1,2,3,4	-	+	-	+
57	66	M	7	1,3	+	+	+	+
58	54	M	6	1,3	-	+	+	-
59	65	F	7	1,3	+	+	-	+
60	77	F	7	1,3,h	+	+	-	-
61	70	F	9	1,2,3,4	+	+	-	-
62	47	F	6	1,3	-	-	-	-
63	49	F	6	1,3	-	+	-	-
64	42	M	7	1,3	-	-	+	-
65	52	M	8	1,2,3	+	+	-	-
66	55	M	13	1,2,3,4,h	+	+	-	-
67	80	F	14	1,2,3,4,h	+	+	-	-
68	63	M	8	1,2,3	+	+	-	+
69	75	F	7	1,2,3	+	+	-	-
70	51	M	8	1,2,3	-	+	+	-
71	45	M	10	1,2,3	-	+	-	-
72	63	F	10	1,2,3,h,v	+	-	-	-
73	55	F	9	1,3,	+	-	-	-
74	54	F	8	1,3	-	+	-	-
75	74	F	8	1,2,3	+	-	-	-

MASTER CHART

SLN	CRP	ESR	UA	F	CT BRAIN SITE OF INFARCT	C/V	BIA	BID	OUTCOME
1	15.6	26	9	449	Right internal Capsule infarct	C	60	70	
2	2.8	10	5	331	Left lacunar infarct	C	85	90	
3	2	12	4	392	Left parietal infarct	C	80	85	
4	25	28	10	300	Right Internal Capsule & corona infarct	C	15	20	
5	8	13	8	556	Corona infarct and right IC infarct	C	15	15	expired
6	6	20	9	350	Left internal capsular infarct	C	60	70	
7	7	12	6	280	Right capsuloganglionic infarct	C	70	80	
8	24	8	10	526	Left Thalamic infarct	C	85	90	
9	15	8	6	440	Left Thalamic infarct	C	85	95	
10	30	30	12	580	Multiinfarct	C	20	20	
11	6	10	5	280	Left lacunar infarct	C	90	95	
12	26	28	12	650	Multiinfarct	C	5	5	expired
13	10	8	4	280	Left cerebellar infarct	V	95	95	
14	15	10	7	560	Bilateral lacunar infarct	C	85	90	
15	15	12	8	240	Left cerebellar infarct	V	95	95	
16	11	16	10	300	left internal capsule infarct	C	20	20	
17	13	4	13	209	left lacunar infarct	C	35	30	
18	5.6	9	14	290	left parietal infarct	C	40	30	
19	3.4	6	9	336	Right capsuloganglionic infarct	C	60	70	
20	10	10	8	345	right thalamic infarct	C	40	45	
21	4.1	9	6	321	right internal capsule infract	C	75	80	
22	6	8	12	445	Left parietal infarct	C	40	45	
23	8.4	5	10	430	right parietal infarct	C	50	55	
24	3	13	12	420	corona radiata infract	C	40	40	
25	12.4	17	11	320	left internal capsule infarct	C	30	30	
26	15	12	8	330	left capsuloganglionic infarct	C	20	20	
27	12.3	10	9	380	left lacunar infarct	C	30	35	
28	11	9	8	290	right lacunar infarct	C	25	30	
29	7.8	8	7	272	multi infarct	C	10	10	expired
30	8	12	8	286	right occipital infarct	C	80	85	
31	7	13	6	350	Left internal capsular infarct	C	55	60	
32	8	12	6	280	right thalamic infarct	C	95	100	
33	16	28	12	290	Left corona radiata infarct	C	50	60	
34	30	34	12	654	Bilateral lacunar infarct	C	50	50	
35	26	28	10	610	Bilateral Capsuloganglionic infarct	C	15	15	expired
36	24	30	9	590	Internal capsular infarct	C	55	60	
37	12	15	18	370	left internal capsule infarct	C	70	70	
38	13	10	8	400	Pontine infarct	V	0	0	expired
39	8	8	5	280	left lacunar infarct	C	80	90	
40	10	10	4	250	right lacunar infarct	C	80	90	
41	30	28	12	557	Left parietal infarct	C	30	40	
42	11	8	12	386	right thalamic infarct	C	95	100	

MASTER CHART

SLN	CRP	ESR	UA	F	CT BRAIN SITE OF INFARCT	C/V	BIA	BID	OUTCOME
43	25	26	14	670	multi infarct	C	10	10	expired
44	16	32	15	580	left internal capsule infarct	C	55	60	
45	13	22	11	420	right parieto occipital infarct	C	60	70	
46	9	13	8	350	Internal capsular infarct	C	70	80	
47	15	22	6	420	Multiple lacunes	C	60	65	
48	14	16	9	432	left capsuloganglionic infarct	C	80	85	
49	28	30	14	670	Bilateral internal capsular infarct	C	0	15	
50	14	18	12	546	corona radiata infract	C	40	45	
51	16	30	14	550	Multi infarct	C	20	20	
52	18	24	12	448	left internal capsule infarct	C	40	45	
53	5	8	6	220	Left lacunar infarct	C	90	100	
54	6	8	7	280	Left lacunar infarct	C	90	100	
55	5.5	10	5	276	Right Centrum semiovale	C	60	70	
56	34	36	13	594	Left internal capsular infarct	C	30	30	
57	10	10	8	360	Left cerebellar infarct	V	85	90	
58	6	6	6	245	Left lacunar infarct	C	90	95	
59	13	18	12	450	left external capsular infarct	C	45	45	
60	15	16	14	521	Multi infarct	C	10	10	
61	30	28	11	550	Multi infarct	C	10	10	expired
62	2.8	6	4	245	Left lacunar infarct	C	80	90	
63	3	6	7	274	Left internal capsular infarct	C	40	50	
64	4	4	5	323	corona radiata infract	C	80	90	
65	9	10	7	348	Right MCA infarct	C	60	70	
66	36	28	10	612	Bilateral infarct	C	10	10	expired
67	28	34	12	564	Bilateral infarct	C	0	0	expired
68	10	8	6	390	Right internal capsular infarct	C	50	60	
69	17	22	8	364	left capsuloganglionic infarct	C	55	60	
70	4	6	4	267	lacunar infarct left	C	90	100	
71	8	12	7	346	Right MCA infarct	C	50	60	
72	26	28	14	490	Left MCA/ACA infact	C	40	40	
73	6	8	6	290	Left thalamic infarct	C	85	95	
74	8	10	5	280	lacunar infarct right	C	90	100	
75	22	24	13	564	Left MCA/ACA infact	C	30	30	

KEY TO MASTER CHART

SLN - SERIAL NUMBER

SEX
M - MALE
F – FEMALE

DURATION : NUMBER OF DAYS

SYMTPOMS
1- HEMIPARESIS/HEMIPLEGIA
2.APHASIA /DYSPHASIA
3.CRANIAL NERVE INVOLVEMENT
4.ALTERED SENSORIUM

H -HEADACHE
V -VOMITTING
S -SEIZURES

DM - DIABETES MELLITUS
HTN - HYPERTENSION

CRP - C-REACTIVE PROTEIN mg/l
ESR - ERYTHROCYTE SEDIMENTATION RATE mm first hr
UA - URIC ACID mg/dL
F -FIBRINOGEN mg/dl

ARTERIAL TERRITORY
C- CAROTID
V- VERTEBRAL

BIA : BARTHEL INDEX AT ADMISSION
BID : BARTHEL INDEX AT DISCHARGE